To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

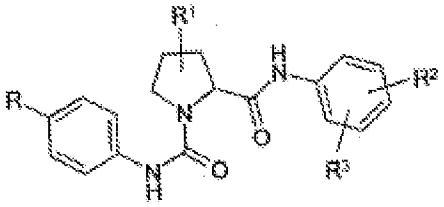
Title of Invention: Method for the production of pyrrolidine-1,2-dicarboxylic acid-1-(phenylC-amide)-2-(phenylC-amide)) Derivatives & 1-(phenylcarbamoyl)-pyrrolidine-2-carboxylic acid derivatives as intermediate

Inventors (please provide full names): Werner Medwski, Christos Tsaklakidis, Dieter Dorsch, Bertram Cezanne & Johannes Gleitz

Earliest Priority Date: 04/03/03

**Listing of Claims:**

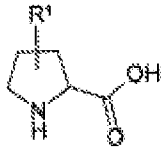
1. (Original) Process for the preparation of compounds of the formula I



I

including mixtures thereof in all ratios, characterised in that

a) a compound of the formula II

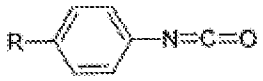


II

in which

$R^1$ is as defined above,

is reacted with a compound of the formula III

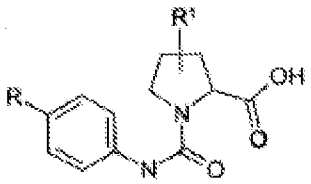


III

in which

R is as defined above,

to give a compound of the formula IV



IV

=> fil reg;dis his nofile;d l5 que stat;fil hcaplus;d 1-16 ibib abs fhit 16

FILE 'REGISTRY' ENTERED AT 15:39:04 ON 18 JUN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 JUN 2008 HIGHEST RN 1028750-52-8
DICTIONARY FILE UPDATES: 17 JUN 2008 HIGHEST RN 1028750-52-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

(FILE 'HOME' ENTERED AT 15:33:08 ON 18 JUN 2008)

FILE 'REGISTRY' ENTERED AT 15:33:26 ON 18 JUN 2008

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L3             STR L1
L4          47 SEA SSS SAM L3
L5         746 SEA SSS FUL L3
               D L5 QUE STAT
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FILE 'HCAPLUS' ENTERED AT 15:37:04 ON 18 JUN 2008

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FILE 'REGISTRY' ENTERED AT 15:39:04 ON 18 JUN 2008

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L3             STR
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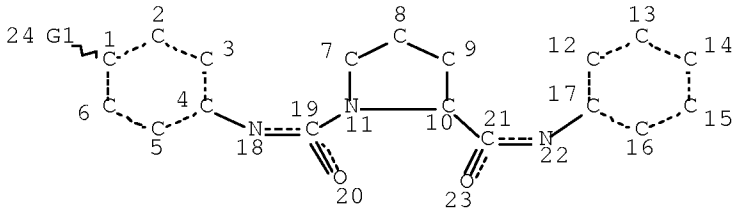
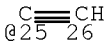




VAR G1=X/25
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L5 746 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED 1364 ITERATIONS 746 ANSWERS
SEARCH TIME: 00.00.01

FILE 'HCAPLUS' ENTERED AT 15:39:04 ON 18 JUN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 18 Jun 2008 VOL 148 ISS 25
FILE LAST UPDATED: 17 Jun 2008 (20080617/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> dis his l6-

(FILE 'REGISTRY' ENTERED AT 15:33:26 ON 18 JUN 2008)

FILE 'HCAPLUS' ENTERED AT 15:37:04 ON 18 JUN 2008
L6 16 S L5/P

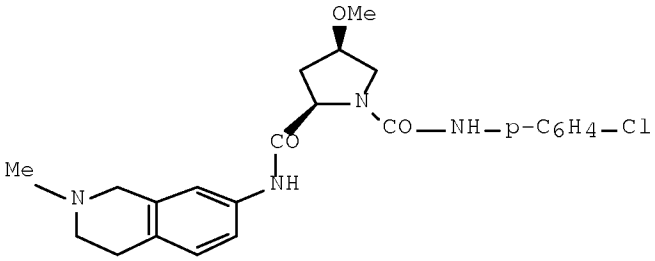
=> d l6 1-16 ibib abs fhitstr

L6 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1334447 HCAPLUS Full-text
DOCUMENT NUMBER: 148:11474
TITLE: Synthesis of substituted prolinamides and their use as Factor Xa and/or serine protease inhibitors
INVENTOR(S): Gerlach, Kai; Priepke, Henning; Pfau, Roland; Wienen, Wolfgang; Schuler-Metz, Annette; Dahmann, Georg; Nar, Herbert
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007131982 | A2 | 20071122 | WO 2007-EP54631 | 20070514 |
| WO 2007131982 | A3 | 20080110 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | | |
| US 20080139605 | A1 | 20080612 | US 2007-749204 | 20070516 |

PRIORITY APPLN. INFO.: EP 2006-113977 A 20060516
EP 2007-102566 A 20070216

OTHER SOURCE(S): MARPAT 148:11474
GI




I

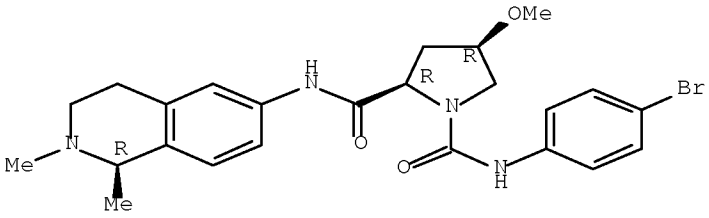
AB Title compds., e.g. (I) as free bases or salts, were prepared as Factor Xa and/or serine protease inhibitors (no data) for treatment of medical disorders (no specified), and recipes for their delivery as ampuls for injection, tablets, capsules, or suppositories are given. Thus, I was prepared starting from (2R,4R)-4-methoxy-pyrrolidin-1,2-dicarbonic acid 1-(1,1-dimethyl)ethyl ester, 4-chloro-Ph isocyanate, and 1,2,3,4-tetrahydro-2-methyl-7-isoquinolinamine, in three steps by first deprotecting the acid group and condensing with the isocyanate, followed by amide formation with the remaining 2-position acid.

IT 957469-66-8P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted prolinamides and their use as Factor Xa and/or serine protease inhibitors)

RN 957469-66-8 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-bromophenyl)-4-methoxy-N2-[(1R)-1,2,3,4-tetrahydro-1,2-dimethyl-6-isoquinolinyl]-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




L6 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

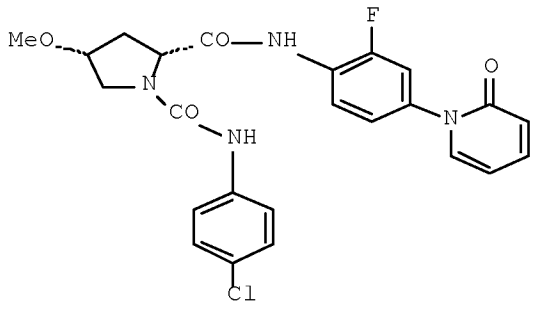
ACCESSION NUMBER: 2007:1004082 HCAPLUS Full-text

DOCUMENT NUMBER: 147:377578

TITLE: The discovery of (2R,4R)-n-(4-chlorophenyl)-n-(2-fluoro-4-(2-oxopyridin-1(2H)-yl)phenyl)-4-methoxypyrrolidine-1,2-dicarboxamide (PD 0348292), an orally efficacious factor Xa inhibitor

AUTHOR(S): Kohrt, Jeffrey T.; Bigge, Christopher F.; Bryant, John W.; Casimiro-Garcia, Agustin; Chi, Liguo; Cody, Wayne L.; Dahring, Tawny; Dudley, Danette A.; Filipski, Kevin J.; Haarer, Staci; Heemstra, Ron; Janiczek, Nancy; Narasimhan, Lakshmi; McClanahan, Thomas; Peterson, J. Thomas; Sahasrabudhe, Vaisheli; Schaum,

Robert; Van Huis, Chad A.; Welch, Kathleen M.; Zhang, Erli; Leadley, Robert J.; Edmunds, Jeremy J.
CORPORATE SOURCE: Michigan Laboratories, Pfizer Global Research & Development, Ann Arbor, MI, 48105, USA
SOURCE: Chemical Biology & Drug Design (2007), 70(2), 100-112
CODEN: CBDDAL; ISSN: 1747-0277
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

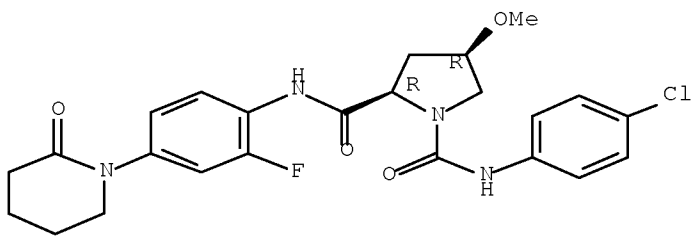


I

AB Herein, we report the discovery of novel, proline-based factor Xa inhibitors containing a neutral P1 chlorophenyl pharmacophore. Through the addnl. incorporation of 1-(4-amino-3-fluoro-phenyl)-1H-pyridin-2-one 22, as a P4 pharmacophore, we discovered compound 7 (PD 0348292, I). This compound is a selective, orally bioavailable, efficacious FXa inhibitor that is currently in phase II clin. trials for the treatment and prevention of thrombotic disorders.

IT 536746-98-2P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pyridinyl pyrrolidines as factor Xa inhibitors)
RN 536746-98-2 HCAPLUS
CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-N2-[2-fluoro-4-(2-oxo-1-piperidinyl)phenyl]-4-methoxy-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:907918 HCAPLUS Full-text
DOCUMENT NUMBER: 147:257637
TITLE: Preparation of 2-pyrrolidinecarboxamides as factor Xa inhibitors
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Gmbh & Co. KG, Germany
SOURCE: Eur. Pat. Appl., 32pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1818330 | A1 | 20070815 | EP 2006-101653 | 20060214 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU | | | | |
| WO 2007093595 | A1 | 20070823 | WO 2007-EP51390 | 20070213 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: EP 2006-101653 A 20060214
OTHER SOURCE(S): MARPAT 147:257637
GI

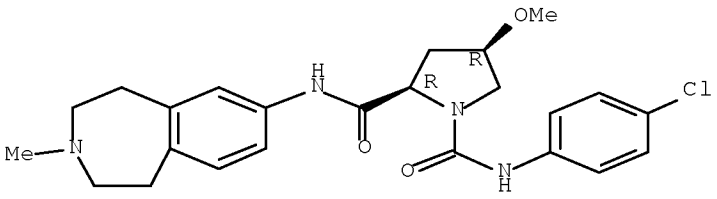
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [K1, K2 = CH2, CO, etc.; K2, K3 = CH2, CO, etc.; X = S, O, CF2, etc.; A1 = N, CR10; A2 = N, CR11; A3 = N, CR12; R10, R11, R12 = H, halo, alkyl, etc.; R3 = H, alkyl; R5 = H, alkyl; R4 and R5 together = CO, CF2, etc.; R13 = H, alkyl; M = Ph, pyridyl, etc.; -L-E-G-J- = C-C-C-C, C-C=C-C] and their pharmaceutically acceptable salts and formulations were prepared For example, N-acylation of pyrrolidine II with 4-chlorophenylisocyanate afforded pyrrolidinecarboxamide III. Compds. I are claimed to be useful as factor Xa inhibitors.

IT 945755-66-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-pyrrolidinecarboxamides as factor Xa inhibitors)

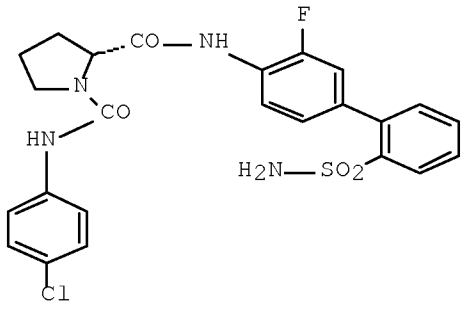
RN 945755-66-8 HCAPLUS
CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-4-methoxy-N2-(2,3,4,5-tetrahydro-3-methyl-1H-3-benzazepin-7-yl)-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:809018 HCAPLUS Full-text
DOCUMENT NUMBER: 147:291356
TITLE: Structure-based drug design of pyrrolidine-1, 2-dicarboxamides as a novel series of orally bioavailable factor Xa inhibitors
AUTHOR(S): Van Huis, Chad A.; Bigge, Christopher F.; Casimiro-Garcia, Agustin; Cody, Wayne L.; Dudley, Danette A.; Filipski, Kevin J.; Heemstra, Ronald J.; Kohrt, Jeffrey T.; Narasimhan, Lakshmi S.; Schaum, Robert P.; Zhang, Erli; Bryant, John W.; Haarer, Staci; Janiczek, Nancy; Leadley, Robert J., Jr.; McClanahan, Thomas; Peterson, J. Thomas; Welch, Kathleen M.; Edmunds, Jeremy J.
CORPORATE SOURCE: Michigan Laboratories, Pfizer Global Research & Development, Ann Arbor, MI, 48105, USA
SOURCE: Chemical Biology & Drug Design (2007), 69(6), 444-450 CODEN: CBDDAL; ISSN: 1747-0277
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI




I

AB A novel series of pyrrolidine-1,2-dicarboxamides was discovered as factor Xa inhibitors using structure-based drug design. This series consisted of a neutral 4-chlorophenylurea P1, a biphenylsulfonamide P4 and a D-proline

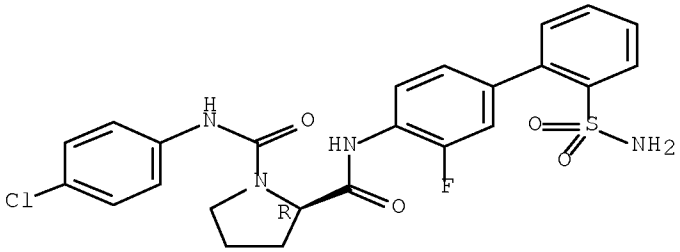
scaffold (I, IC50 = 18 nM). Optimization of the initial hit resulted in an orally bioavailable, subnanomolar inhibitor of factor Xa (13, IC50 = 0.38 nM), which was shown to be efficacious in a canine electrolytic model of thrombosis with minimal bleeding.

IT 536746-25-5P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pyrrolidine dicarboxamides as orally bioavailable factor Xa inhibitors)

RN 536746-25-5 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N2-[2'-(aminosulfonyl)-3-fluoro[1,1'-biphenyl]-4-yl]-N1-(4-chlorophenyl)-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1006402 HCAPLUS Full-text

DOCUMENT NUMBER: 145:377210

TITLE: Preparation of polymorphic crystalline forms of N1-(4-chlorophenyl)-N2-[2-fluoro-4-(2-oxo-1(2H)-pyridinyl)phenyl]-4-methoxy-(2R,4R)-1,2-pyrrolidinedicarboxamide factor Xa inhibitor

INVENTOR(S): Samas, Brian Matthew; Vrieze, Derek Clinton

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

SOURCE: PCT Int. Appl., 31pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006100565 | A1 | 20060928 | WO 2006-IB633 | 20060313 |

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | | | |
|---|---|---|---|---|---|
| AU 2006226043 | A1 | 20060928 | AU 2006-226043 | | 20060313 |
| CA 2602550 | A1 | 20060928 | CA 2006-2602550 | | 20060313 |
| EP 1891044 | A1 | 20080227 | EP 2006-727345 | | 20060313 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | | |
| JP 2006265254 | A | 20061005 | JP 2006-81926 | | 20060324 |
| IN 2007DN06355 | A | 20070831 | IN 2007-DN6355 | | 20070816 |
| KR 2007107156 | A | 20071106 | KR 2007-721901 | | 20070921 |
| CN 101146792 | A | 20080319 | CN 2006-80009365 | | 20070921 |
| PRIORITY APPLN. INFO.: | | | US 2005-664870P | P | 20050324 |
| | | | WO 2006-IB633 | W | 20060313 |

OTHER SOURCE(S): CASREACT 145:377210

AB Polymorphic crystalline forms of N1-(4-chlorophenyl)-N2-[2-fluoro-4-(2-oxo-1(2H)-pyridinyl)phenyl]-4-methoxy-(2R,4R)-1,2-pyrrolidinedicarboxamide factor Xa inhibitor are prepared and characterized by their powder X-ray diffraction, solid-state NMR, etc., and pharmaceutical dosage forms containing it are claimed.

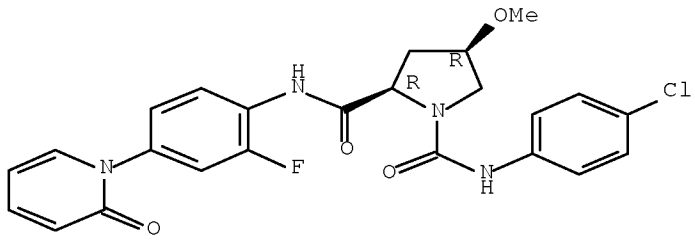
IT 536748-46-6P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polymorphic crystalline forms of N1-(4-chlorophenyl)-N2-[2-fluoro-4-(2-oxo-1(2H)-pyridinyl)phenyl]-4-methoxy-(2R,4R)-1,2-pyrrolidinedicarboxamide factor Xa inhibitor)

RN 536748-46-6 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-N2-[2-fluoro-4-(2-oxo-1(2H)-pyridinyl)phenyl]-4-methoxy-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

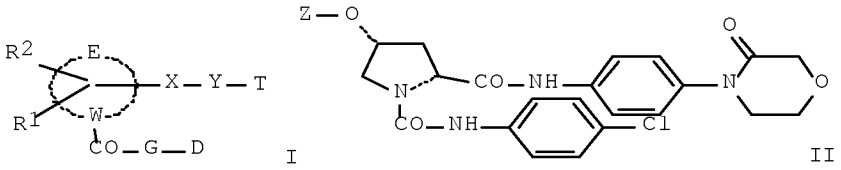
L6 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2006:316811 HCAPLUS Full-text |
| DOCUMENT NUMBER: | 144:370085 |
| TITLE: | Preparation of 1,2-pyrrolidinedicarboxamides as coagulation factor Xa inhibitors |
| INVENTOR(S): | Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes |
| PATENT ASSIGNEE(S): | Merck Patent G.m.b.H., Germany |
| SOURCE: | PCT Int. Appl., 103 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | German |

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006034769 | A1 | 20060406 | WO 2005-EP9418 | 20050901 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| DE 102004047254 | A1 | 20060413 | DE 2004-102004047254 | 20040929 |
| AU 2005289164 | A1 | 20060406 | AU 2005-289164 | 20050901 |
| CA 2581732 | A1 | 20060406 | CA 2005-2581732 | 20050901 |
| EP 1797071 | A1 | 20070620 | EP 2005-790356 | 20050901 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 101031561 | A | 20070905 | CN 2005-80032789 | 20050901 |
| JP 2008514655 | T | 20080508 | JP 2007-533891 | 20050901 |
| MX 200703470 | A | 20070510 | MX 2007-3470 | 20070323 |
| KR 2007057878 | A | 20070607 | KR 2007-707053 | 20070328 |
| US 20080081814 | A1 | 20080403 | US 2007-576207 | 20070328 |
| IN 2007KN01474 | A | 20070720 | IN 2007-KN1474 | 20070425 |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004047254A | 20040929 |
| | | | WO 2005-EP9418 W | 20050901 |

OTHER SOURCE(S): MARPAT 144:370085
GI




I II

AB Title compds. I [R1, R2 = H, =O, halo, etc.; R3 = H, CH2CH(OH)CH2OH, CH2CH(OH)CH2NH2, etc.; W = N, CR3 with provisos, etc.; E = together with W form a 3 to 7-membered hetero or carbocyclic ring with provisos; D = bond, double bond, etc.; G = [C(R4)2]n, [C(R4)2]nNR3, [C(R4)2]nO, etc.; R4 = H, A; A =alkyl with provisos; X = [C(R4)2]nCONR3[C(R4)2]n, etc.; n = 0-2; Y = alkylene, cycloalkylene, etc.; T = bond, double bond, heterocycle with provisos, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, O-acylation of hydroxypyrrolidine II [Z = H] afforded pyrrolidinedicarboxamide II [Z = CO2Et]. In coagulation factor Xa inhibition assays, pyrrolidinedicarboxamide II [Z = CO2Et] exhibited an IC50 value of 2.0x10-9 M.

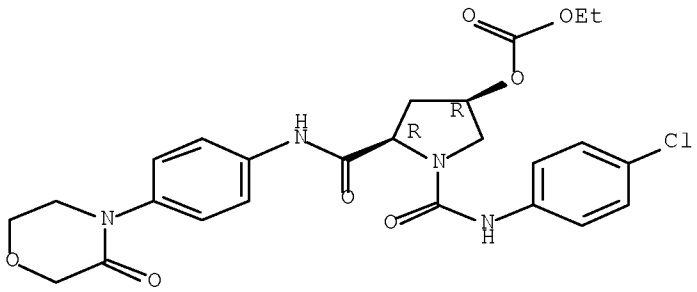
IT 882066-89-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinedicarboxamides as coagulation factor xa inhibitors)

RN 882066-89-9 HCAPLUS

CN Carbonic acid, (3R,5R)-1-[[(4-chlorophenyl)amino]carbonyl]-5-[[[4-(3-oxo-4-morpholinyl)phenyl]amino]carbonyl]-3-pyrrolidinyl ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:273940 HCAPLUS Full-text

DOCUMENT NUMBER: 144:331461

TITLE: Drugs containing carbonyl compounds and their use for the prophylaxis and/or therapy of thromboembolic illnesses

INVENTOR(S): Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Ger. Offen., 77 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

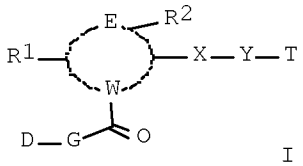
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 102004045796 | A1 | 20060323 | DE 2004-102004045796 | 20040922 |
| AU 2005287637 | A1 | 20060330 | AU 2005-287637 | 20050824 |
| CA 2581172 | A1 | 20060330 | CA 2005-2581172 | 20050824 |
| WO 2006032342 | A2 | 20060330 | WO 2005-EP9124 | 20050824 |
| WO 2006032342 | A3 | 20070111 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
EP 1791597 A2 20070606 EP 2005-774750 20050824
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
BA, HR, MK, YU
CN 101102818 A 20080109 CN 2005-80031723 20050824
JP 2008513387 T 20080501 JP 2007-531628 20050824
MX 200703175 A 20070518 MX 2007-3175 20070316
KR 2007054210 A 20070528 KR 2007-706440 20070321
US 20080003214 A1 20080103 US 2007-575711 20070321
IN 2007KN01362 A 20070720 IN 2007-KN1362 20070418
PRIORITY APPLN. INFO.: DE 2004-102004045796A 20040922
WO 2005-EP9124 W 20050824
OTHER SOURCE(S): MARPAT 144:331461
GI

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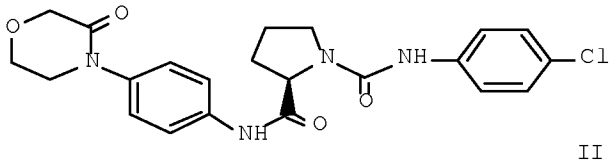



II

AB Use of heterocyclic carbonyl compds. I [R1, R2 = H, :O,,halogen, A, C.tplbond.CH, OR3,N(R3)2, NO2, CN, N3, CO2R3, CON(R3)2, [C(R4)2]n-Ar, [C(R4)2]n-heterocyclyl, [C(R4)2]n-cycloalkyl, OC(:O)R3, OC(:O)N(R3)2, NR3COA, NR3SO2A; R1R2 = bi- or spirocyclic 3- to 7-membered carbocycle or heterocycle (containing 0 - 3 N, O, or S); R3 = H, A, CH2C.tplbond.CH, CH2CH(OH)CH2OH, CH2CH(OH)CH2NH2, CH2CH(OH)CH2-heterocycle, [C(R4)2]n-Ar, [C(R4)2]n-heterocyclyl, [C(R4)2]n-cycloalkyl, [C(R4)2]n-CO2A, [C(R4)2]nN(R4)2; R4 = H, A; EW = 3- to 7-membered carbocycle or heterocycle (containing 0 - 3 N, O, or S); W = N, CR3, sp2-C; D = mono- or binuclear, (un)substituted aromatic carbocycle or heterocycle (containing 0 - 3 N, O, or S); G = [C(R4)2]n, [C(R4)2]n-NR3, [C(R4)2]nO, [C(R4)2]nS, [CR4:CR4]n; X = [C(R4)2]nCONR3[C(R4)2]n, [C(R4)2]nNR3CO[C(R4)2]n, [C(R4)2]nNR3[C(R4)2]n, [C(R4)2]nO[C(R4)2]n, [C(R4)2]nC(:O)[C(R4)2]n, [C(R4)2]nCO2[C(R4)2]n; Y = alkylene, cycloalkylene, heterodiyl, aryldiyl; T = mono- or binuclear, (un)substituted aromatic carbocycle or heterocycle (containing 0 - 3 N, O, or S); A = (un)branched C1-10-alkyl (optionally containing, O, S or CH:CH in the chain and replacing 1 - 7 H with F); n = 0 - 2; o = 1 - 3], their derivs., solvates, salts and stereoisomers, for the prophylaxis and/or therapy of thromboembolic illnesses. Thus, proline derivative II was prepared from N-Boc-D-proline via amidation with 4-(4-aminophenyl)morpholin-3-one in DMF containing 1-hydroxybenzotriazole hydrate, N-[3-(dimethylamino)propyl]-N'-

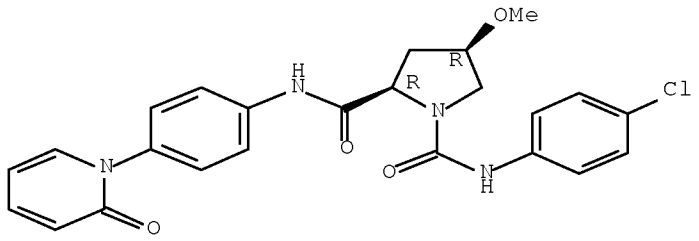
ethylcarbodiimide hydrochloride and N-methylmorpholine, N-deprotection with aqueous HClin dioxane and carbamylation with 4-ClC6H4NCO in CH2Cl2 containing Et3N. The receptor binding activity of II was determined [IC50 = 1.8 x 10-8 M vs. FXa; IC50 = 2.3 x 10-8 M vs. TF/FVIIa].

IT 536747-22-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drugs containing carbonyl compds. and their use for the prophylaxis and/or therapy of thromboembolic illnesses)

RN 536747-22-5 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-4-methoxy-N2-[4-(2-oxo-1(2H)-pyridinyl)phenyl]-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




L6 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1075769 HCAPLUS Full-text

DOCUMENT NUMBER: 143:347450

TITLE: Synthesis of prolinyl derivatives for use in the treatment of thromboembolic diseases or tumors

INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005092849 | A1 | 20051006 | WO 2005-EP2306 | 20050304 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 102004014945 | A1 | 20051013 | DE 2004-102004014945 | 20040326 |
| AU 2005225489 | A1 | 20051006 | AU 2005-225489 | 20050304 |

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|---|---|---|---|---|
| CA 2561057 | A1 | 20051006 | CA 2005-2561057 | 20050304 |
| EP 1735279 | A1 | 20061227 | EP 2005-715737 | 20050304 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LV | | | | |
| CN 1938269 | A | 20070328 | CN 2005-80009735 | 20050304 |
| BR 2005009174 | A | 20070918 | BR 2005-9174 | 20050304 |
| JP 2007530469 | T | 20071101 | JP 2007-504284 | 20050304 |
| IN 2006KN02397 | A | 20070525 | IN 2006-KN2397 | 20060824 |
| MX 2006PA10771 | A | 20061215 | MX 2006-PA10771 | 20060920 |
| KR 2007010131 | A | 20070122 | KR 2006-719772 | 20060925 |
| US 20070135507 | A1 | 20070614 | US 2006-594024 | 20060925 |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004014945A | 20040326 |
| | | | WO 2005-EP2306 W | 20050304 |

OTHER SOURCE(S): MARPAT 143:347450

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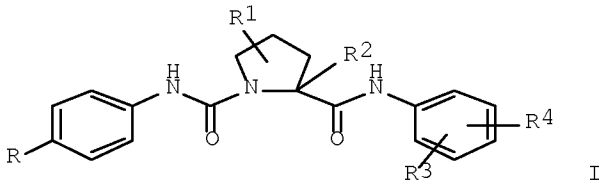

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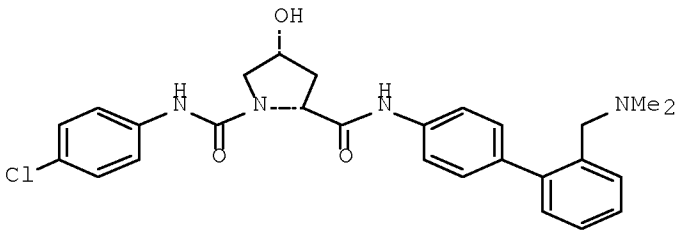


II

AB The invention relates to title compds., e.g. (I), which are inhibitors of coagulation factors Xa and VIIa and can be used for the prophylaxis and/or treatment of thromboembolic diseases and for the treatment of tumors (no data). Thus, (II) was prepared by condensation of (2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxylic acid 1-tert-Bu ester with 4'-amino-N,N-dimethyl-[1,1'-biphenyl]-2-methanamine, followed by condensation with 4-nitrophenyl chloroformate and 4-chloroaniline, to give II (no yield). Sixteen title compds. are claimed, and formulations for administration (e.g., injections, suppositories, etc.) are given.

IT 865853-86-7P

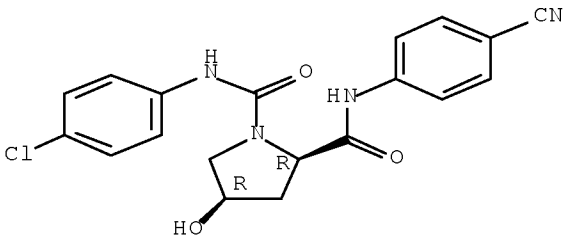
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of proline derivs. for treatment of thromboembolic diseases or tumors)

RN 865853-86-7 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-N2-(4-cyanophenyl)-4-hydroxy-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:564637 HCAPLUS Full-text
DOCUMENT NUMBER: 143:97636
TITLE: Synthesis of prolinylarylacetamides as coagulation factor Xa inhibitors for use in the prevention or treatment of thromboembolic diseases or tumors
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005058817 | A1 | 20050630 | WO 2004-EP13509 | 20041126 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10358814 | A1 | 20050721 | DE 2003-10358814 | 20031216 |
| AU 2004299197 | A1 | 20050630 | AU 2004-299197 | 20041126 |
| CA 2549589 | A1 | 20050630 | CA 2004-2549589 | 20041126 |
| EP 1697318 | A1 | 20060906 | EP 2004-820404 | 20041126 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| CN 1894210 | A | 20070110 | CN 2004-80037698 | 20041126 |
| BR 2004017630 | A | 20070327 | BR 2004-17630 | 20041126 |
| JP 2007513988 | T | 20070531 | JP 2006-544256 | 20041126 |
| IN 2006KN01579 | A | 20070504 | IN 2006-KN1579 | 20060608 |
| MX 2006PA06740 | A | 20060818 | MX 2006-PA6740 | 20060614 |
| US 20070185189 | A1 | 20070809 | US 2006-583094 | 20060615 |
| PRIORITY APPLN. INFO.: | | | DE 2003-10358814 A | 20031216 |
| | | | WO 2004-EP13509 W | 20041126 |

OTHER SOURCE(S): MARPAT 143:97636

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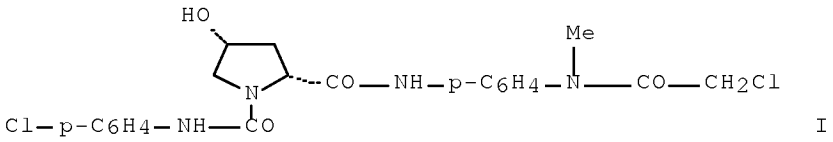


I

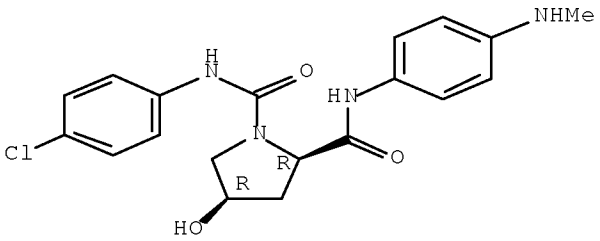
AB Title compds., e.g. (I), are claimed as inhibitors of coagulation factor Xa and are claimed for use for the prophylaxis and/or therapy of thromboembolic diseases and in the treatment of tumors, as well as kits containing the compds. of interest. Thus, the title compds. were prepared, e.g., by condensation of (2R,4R)-1-(4-chlorophenylcarbamoyl)-4- hydroxyproline and N-(4-aminophenyl)2-dimethylamino-N-Me acetamide in DMF using N-(3-dimethylaminopropyl)-N'-ethyl-carbodiimide hydrochloride as condensing agent. In pharmacol. testing, I had receptor affinity IC50 values of 17.0 nM and 25.0 M using FXa and TF/FVIIa receptors, resp. (no details given). Various formulations for administering the title compds. therapeutically are given.

IT 855855-29-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of prolinylarylacetamides as coagulation factor Xa inhibitors for prevention or treatment of thromboembolic diseases or tumors)

RN 855855-29-7 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-4-hydroxy-N2-[4-(methylamino)phenyl]-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1124627 HCAPLUS Full-text

DOCUMENT NUMBER: 142:74838

TITLE: Preparation of pyrrolidin-1,2-dicarboxylic acids and related compounds as coagulation factor Xa and factor VIIa inhibitors

INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004110433 | A1 | 20041223 | WO 2004-EP5717 | 20040527 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10327428 | A1 | 20050105 | DE 2003-10327428 | 20030618 |
| DE 10329457 | A1 | 20050120 | DE 2003-10329457 | 20030701 |
| AU 2004246766 | A1 | 20041223 | AU 2004-246766 | 20040527 |
| CA 2529453 | A1 | 20041223 | CA 2004-2529453 | 20040527 |
| EP 1633346 | A1 | 20060315 | EP 2004-735007 | 20040527 |
| EP 1633346 | B1 | 20060823 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004011466 | A | 20060711 | BR 2004-11466 | 20040527 |
| CN 1809346 | A | 20060726 | CN 2004-80016955 | 20040527 |
| AT 337000 | T | 20060915 | AT 2004-735007 | 20040527 |
| JP 2006527708 | T | 20061207 | JP 2006-515798 | 20040527 |
| ES 2271894 | T3 | 20070416 | ES 2004-735007 | 20040527 |
| IN 2005KN02399 | A | 20070727 | IN 2005-KN2399 | 20051128 |
| MX 2005PA13536 | A | 20060309 | MX 2005-PA13536 | 20051213 |
| US 20070093472 | A1 | 20070426 | US 2005-561227 | 20051219 |

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|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 2003-10327428 | A | 20030618 |
| | DE 2003-10329457 | A | 20030701 |
| | WO 2004-EP5717 | W | 20040527 |

OTHER SOURCE(S): MARPAT 142:74838
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R = H, X, A, etc.; R1 = H, =O, halo, etc.; R2 = H, halo, A; R3 = (un)substituted aromatic heterocycle containing 1-4 N, O, S atoms; X = aryl, arylalkyl, het, etc.; A = (un)substituted cycloalkyl] and their pharmaceutically acceptable salts and formulations were prepared For example, condensation of proline II, e.g., prepared from BOC-methoxyproline in 3-steps, and 4-nitrophenylchloroformate and 4-ethynylaniline afforded claimed pyrrolidinyldicarboxylic III in 40% yield. In coagulation factor Xa receptor affinity binding assays, 14-examples of compds. I exhibited IC50 values ranging from 1.1-4.8 nM, i.e., the IC50 value of pyrrolidinyldicarboxylic III was 1.3 nM. Compds. I are claimed to be useful as factor Xa and factor VIIa inhibitors for the treatment of thromboembolic diseases.

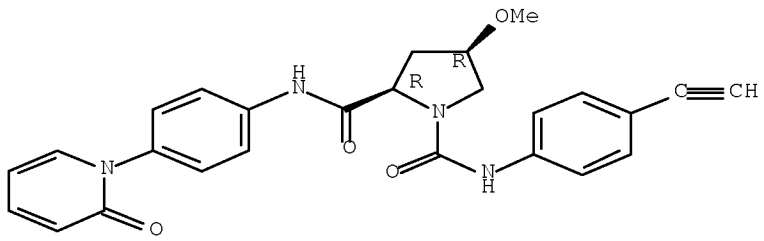
IT 814263-98-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolidinyldicarboxylic acids and related compds. as factor Xa and factor VIIa inhibitors)

RN 814263-98-4 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-ethynylphenyl)-4-methoxy-N2-[4-(2-oxo-1(2H)-pyridinyl)phenyl]-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:857591 HCAPLUS Full-text

DOCUMENT NUMBER: 141:314626

TITLE: Method for the production of pyrrolidine-1,2-dicarboxylic acid-1-(phenyl(-amide))-2-(phenyl(-amide)) derivatives and 1-(phenylcarbamoyl)-pyrrolidine-2-carboxylic acid derivatives as intermediate products

INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany

SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004087695 | A1 | 20041014 | WO 2004-EP2405 | 20040309 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| DE 10327428 | A1 | 20050105 | DE 2003-10327428 | 20030618 |
| DE 10329295 | A1 | 20050203 | DE 2003-10329295 | 20030630 |
| DE 10329457 | A1 | 20050120 | DE 2003-10329457 | 20030701 |
| DE 10334174 | A1 | 20050217 | DE 2003-10334174 | 20030726 |

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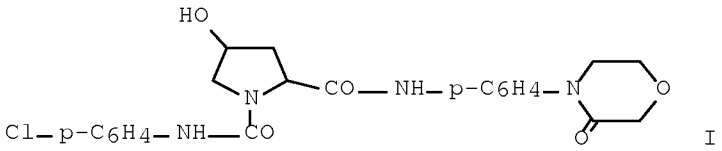
|---|---|---|---|---|---|
| AU 2004226280 | A1 | 20041014 | AU 2004-226280 | | 20040309 |
| CA 2520893 | A1 | 20041014 | CA 2004-2520893 | | 20040309 |
| EP 1608646 | A1 | 20051228 | EP 2004-718646 | | 20040309 |
| EP 1608646 | B1 | 20070711 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | | |
| BR 2004008888 | A | 20060411 | BR 2004-8888 | | 20040309 |
| JP 2006522037 | T | 20060928 | JP 2006-504602 | | 20040309 |
| EP 1760081 | A1 | 20070307 | EP 2006-22891 | | 20040309 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LT, LV | | | | | |
| US 20060211692 | A1 | 20060921 | US 2005-551670 | | 20050930 |
| IN 2005KN02182 | A | 20060929 | IN 2005-KN2182 | | 20051103 |
| PRIORITY APPLN. INFO.: | | | DE 2003-10315377 | A | 20030403 |
| | | | DE 2003-10327428 | A | 20030618 |
| | | | DE 2003-10329295 | A | 20030630 |
| | | | DE 2003-10329457 | A | 20030701 |
| | | | DE 2003-10334174 | A | 20030726 |
| | | | EP 2004-718646 | A3 | 20040309 |
| | | | WO 2004-EP2405 | W | 20040309 |

OTHER SOURCE(S): CASREACT 141:314626; MARPAT 141:314626

GI

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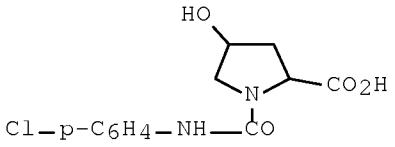



II

AB The invention relates to a method for the production of title compds., e.g. (I), and intermediate products, e.g. (II) for the production of I. Thus, cis-hydroxy-D-proline was reacted with 4-chlorophenylisocyante in NaHCO3 at 80° for 5 h. to give after workup 81.8% (R,R)-II. II was then reacted with 4-(3-oxo-4-morpholinyl)aniline in THF with 2-ethoxy-1(2H)-quinolinecarboxylic acid Et ester (EEDQ) as coupling agent at room temperature for 20 h to give, after workup, 69% (R,R)-I.

IT 768370-75-8P

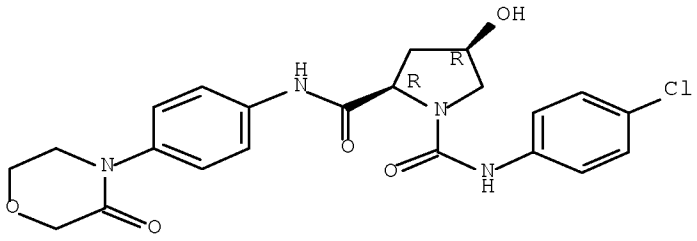
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of substituted Ph 1,2-pyrrolidinedicarboxylic acid diamides and intermediates)

RN 768370-75-8 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-4-hydroxy-N2-[4-(3-oxo-4-morpholinyl)phenyl]-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

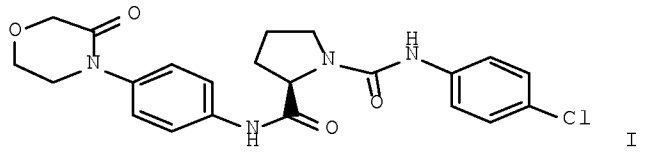
L6 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:857551 HCAPLUS Full-text
DOCUMENT NUMBER: 141:350179
TITLE: Preparation of azolidinedicarboxamides and related compounds as Factor Xa and Factor VIIa inhibitors
INVENTOR(S): Tsaklakidis, Christos; Dorsch, Dieter; Mederski, Werner; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004087646 | A2 | 20041014 | WO 2004-EP2350 | 20040308 |
| WO 2004087646 | A3 | 20050106 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| DE 10329295 | A1 | 20050203 | DE 2003-10329295 | 20030630 |
| AU 2004226278 | A1 | 20041014 | AU 2004-226278 | 20040308 |
| CA 2521069 | A1 | 20041014 | CA 2004-2521069 | 20040308 |
| BR 2004008420 | A | 20060321 | BR 2004-8420 | 20040308 |
| JP 2006522033 | T | 20060928 | JP 2006-504581 | 20040308 |
| EP 1720844 | A2 | 20061115 | EP 2004-718299 | 20040308 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LT, LV | | | | |
| IN 2005KN01684 | A | 20070727 | IN 2005-KN1684 | 20050823 |
| US 20060183739 | A1 | 20060817 | US 2005-551557 | 20051003 |

PRIORITY APPLN. INFO.: DE 2003-10315377 A 20030403
DE 2003-10329295 A 20030630

US 2003-483897P P 20030702
WO 2004-EP2350 W 20040308

OTHER SOURCE(S): MARPAT 141:350179
GI



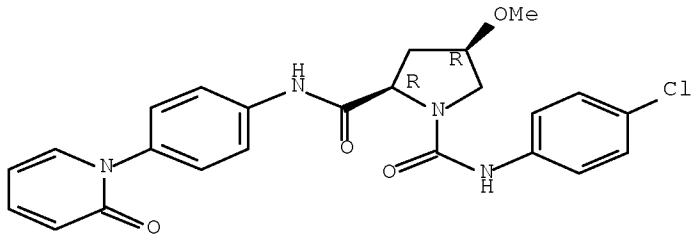
I

AB R1R2(TYX)EWCOGD [R1, R2 = H, O, halo, A, ethynyl, OR3, N(R3)2, NO2, cyano, N3, CO2R3, CON(R3)2, etc.; R3 = H, A, HC.tplbond.CCH2, MeC.tplbond.CCH2, CH2CH(OH)CH2OH, etc.; R4 = H, A; W = N, C, CR3; E = atoms to form a 3-7 membered (heterocyclic) ring optionally containing a double bond; D = mono- or dinuclear (substituted) (hetero)aryl; G = [C(R4)2]n, [C(R4)2]nNR3, [C(R4)2]nO, [C(R4)2]nS, etc.; n = 0-2; X = [C(R4)2]nCO[C(R4)2]n, [C(R4)2]n,NR3[C(R4)2]n, [C(R4)2]nNR3CO[C(R4)2]n, etc.; Y = alkylene, cycloalkylene, heterocyclylene, arenediyl; T = substituted mono- or dinuclear carbocyclyl, heterocyclyl; A = (fluoro-substituted) alkyl optionally interrupted by O, S, CH:CH], were prepared Thus, title compound (I) [preparation from 4-(4-aminophenyl)morpholin-3-one, Boc-D-proline, and 4-chlorophenyl isocyanate given] bound to Factor Xa receptors with IC50 = 1.8 + 10-8 M.

IT 536747-22-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azolidinedicarboxamides and related compds. as Factor Xa and Factor VIIa inhibitors)

RN 536747-22-5 HCAPLUS
CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-4-methoxy-N2-[4-(2-oxo-1(2H)-pyridinyl)phenyl]-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:841766 HCAPLUS Full-text
DOCUMENT NUMBER: 141:332202
TITLE: Preparation of azolidinecarboxamides as antithrombotics and anticancer drugs.
INVENTOR(S): Tsaklakidis, Christos; Dorsch, Dieter; Mederski, Werner; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany

SOURCE: Ger. Offen., 47 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| AU 2004226278 | A1 | 20041014 | AU 2004-226278 | 20040308 |
| CA 2521069 | A1 | 20041014 | CA 2004-2521069 | 20040308 |
| WO 2004087646 | A2 | 20041014 | WO 2004-EP2350 | 20040308 |
| WO 2004087646 | A3 | 20050106 | | |
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| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2004008420 | A | 20060321 | BR 2004-8420 | 20040308 |
| CN 1771237 | A | 20060510 | CN 2004-80009354 | 20040308 |
| JP 2006522033 | T | 20060928 | JP 2006-504581 | 20040308 |
| EP 1720844 | A2 | 20061115 | EP 2004-718299 | 20040308 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LT, LV | | | | |
| AU 2004226280 | A1 | 20041014 | AU 2004-226280 | 20040309 |
| AU 2004226281 | A1 | 20041014 | AU 2004-226281 | 20040309 |
| CA 2520893 | A1 | 20041014 | CA 2004-2520893 | 20040309 |
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| WO 2004087695 | A1 | 20041014 | WO 2004-EP2405 | 20040309 |
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| WO 2004087696 | A1 | 20041014 | WO 2004-EP2407 | 20040309 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1608645 | A1 | 20051228 | EP 2004-718641 | 20040309 |

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| EP 1608646 | B1 | 20070711 | | | | |
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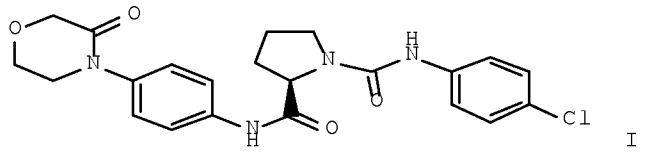
| BR 2004008444 | A | 20060404 | BR 2004-8444 | | 20040309 | |
| BR 2004008888 | A | 20060411 | BR 2004-8888 | | 20040309 | |
| CN 1771248 | A | 20060510 | CN 2004-80009374 | | 20040309 | |
| CN 1771249 | A | 20060510 | CN 2004-80009463 | | 20040309 | |
| JP 2006522037 | T | 20060928 | JP 2006-504602 | | 20040309 | |
| JP 2006522038 | T | 20060928 | JP 2006-504604 | | 20040309 | |
| AT 361296 | T | 20070515 | AT 2004-718641 | | 20040309 | |
| AT 366732 | T | 20070815 | AT 2004-718646 | | 20040309 | |
| ES 2285444 | T3 | 20071116 | ES 2004-718641 | | 20040309 | |
| ES 2287708 | T3 | 20071216 | ES 2004-718646 | | 20040309 | |
| IN 2005KN01684 | A | 20070727 | IN 2005-KN1684 | | 20050823 | |
| US 20060211692 | A1 | 20060921 | US 2005-551670 | | 20050930 | |
| US 20060183739 | A1 | 20060817 | US 2005-551557 | | 20051003 | |
| US 20060183742 | A1 | 20060817 | US 2005-551559 | | 20051003 | |
| IN 2005KN02182 | A | 20060929 | IN 2005-KN2182 | | 20051103 | |
| IN 2005KN02183 | A | 20070323 | IN 2005-KN2183 | | 20051103 | |
| PRIORITY APPLN. INFO.: | | | DE 2003-10315377 | A | 20030403 | |
| | | | DE 2003-10327428 | A | 20030618 | |
| | | | DE 2003-10329295 | A | 20030630 | |
| | | | DE 2003-10329457 | A | 20030701 | |
| | | | US 2003-483897P | P | 20030702 | |
| | | | DE 2003-10334174 | A | 20030726 | |
| | | | DE 2003-10336570 | A | 20030808 | |
| | | | WO 2004-EP2350 | W | 20040308 | |
| | | | WO 2004-EP2405 | W | 20040309 | |
| | | | WO 2004-EP2407 | W | 20040309 | |

OTHER SOURCE(S): MARPAT 141:332202

GI



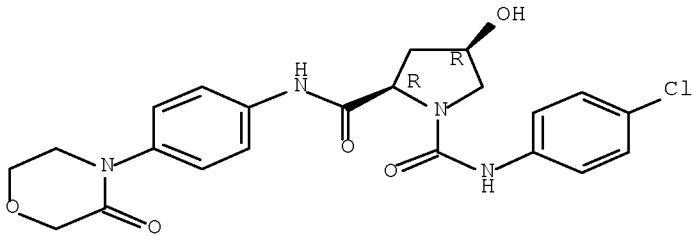
I

AB R1R2(TYX)EWCOGD [R1, R2 = H, O, halo, A, ethynyl, OR3, NO2, cyano, N3, CO2R3, CON(R3)2, NR3COA, NR3SO2A, etc.; R1R2 = toms to form a bicyclic or spirocyclic (heterocyclic) ring; R3 = H, A, etc.; R4 = H, A; W = N, CR3, C; E = atoms to form a 3-7 membered (double bond containing) (heterocyclic) ring with W; G = [C(R4)2]n, [C(R4)2]nNR3, [C(R4)2]nO, [C(R4)2]nS; X = [C(R4)2]nCONR3[C(R4)2]n, [C(R4)2]nON[C(R4)2]n, etc.; Y = alkylene, cycloalkylene, (substituted) heterocyclylene, arylene; T = mono- or bicyclic substituted (unsatd.) (hetero)cyclyl; A = (fluoro-substituted) alkylene optionally interrupted by O, S, CH:CH; n = 0-2], were prepared Thus, title compound (I) (prepared from 4-(4-aminophenyl)morpholin-3-one, Boc-D-proline, and 4-chlorophenyl isocyanate), bound to Factor Xa receptors with IC50 = 1.8 + 10-8 M.

IT 768370-75-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of azolidinecarboxamides as antithrombotics and
anticancer drugs)
RN 768370-75-8 HCAPLUS
CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-4-hydroxy-N2-[4-(3-oxo-4-morpholinyl)phenyl]-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




L6 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:799558 HCAPLUS Full-text
DOCUMENT NUMBER: 141:296012
TITLE: Preparation of factor Xa- and thrombin-inhibiting substituted benzamidines and sulfonylbenzamidines as potential anticoagulants
INVENTOR(S): Pinto, Donald J.; Qiao, Jennifer X.; Gangor, Timur; Lam, Patrick Y. S.; Li, Yun-long
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 279 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004083174 | A2 | 20040930 | WO 2004-US8033 | 20040317 |
| WO 2004083174 | A3 | 20041125 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 20040209863 | A1 | 20041021 | US 2004-801518 | 20040316 |
| US 7122557 | B2 | 20061017 | | |
| EP 1603562 | A2 | 20051214 | EP 2004-757516 | 20040317 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK
PRIORITY APPLN. INFO.: US 2003-455709P P 20030318
US 2004-801518 A 20040316
WO 2004-US8033 W 20040317
OTHER SOURCE(S): MARPAT 141:296012
GI

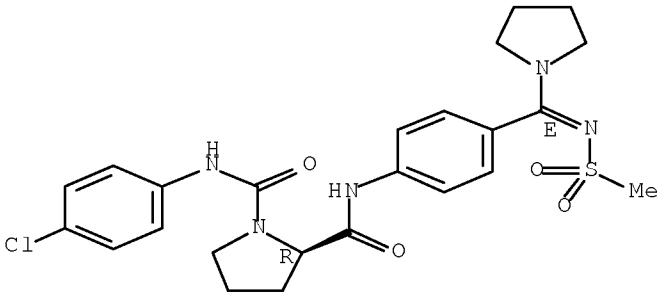
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. P4-M-M4 (I) [M = (un)substituted 3-10 membered carbocyclic or a 4-10 membered heterocyclic ring containing 1-3 O, N, or S atoms, alone or fused to an (un)substituted 5-7 membered carbocycle or heterocycle; P4 = Z-A-B; M4 = G-G1; A = (un)substituted 3-10 membered carbocyclic or 5-12 membered heterocyclic ring ; B = (un)substituted amidino, guanidino, iminomethyl; G = five or six-membered carbocycle or heterocycle fused to a benzene, pyridine, pyrimidine, pyrazine, or pyridazine ring; G1 = bond, (un)substituted alkyl, alkenyl, alkynyl; Z = (un)substituted alkylene], such as tetrahydropyrazolo[3,4-c]pyridinone II or (pyridinylaminocarbonylphenylaminocarbonyl)benzamidine III are prepared as inhibitors of Factor Xa and thrombin for use as anticoagulants. Deprotonation of 2-amino-4-chloropyridine and addition to 5-chloroisatoic anhydride yields N-(5-chloro-2-pyridinyl) 2-amino-5-chlorobenzamide (IV). Acid-mediated addition of dimethylamine to the nitrile of Me 4-cyanobenzoate, mesylation of the amidine nitrogen, and base-mediated hydrolysis of the ester yields 4-(N,N-dimethyl-N'-methylsulfonylamidino)benzoic acid (V). Coupling of IV and V mediated by BOP yields III. Some compds. of the invention inhibit human factor Xa with Ki values of ≤ 10 μM; in addition, some of the invention compds. inhibit thrombin in vitro. (no data).

IT 764658-81-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of factor Xa- and thrombin-inhibiting substituted benzamidines and sulfonylbenzamidines as potential anticoagulants)

RN 764658-81-3 HCAPLUS
CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-N2-[4-[(E)-[(methylsulfonyl)imino]-1-pyrrolidinylmethyl]phenyl]-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:434528 HCAPLUS Full-text
DOCUMENT NUMBER: 139:6763
TITLE: Preparation of pyrrolidinedicarboxamides and related compounds as inhibitors of factor Xa useful for thrombotic disorders
INVENTOR(S): Bigge, Christopher Franklin; Dudley, Danette Andrea; Edmunds, Jeremy John; Van Huis, Chad Alan; Casimiro-Garcia, Agustin; Filipski, Kevin James; Kohrt, Jeffrey Thomas
PATENT ASSIGNEE(S): Warner-Lambert Company L.L.C., USA
SOURCE: PCT Int. Appl., 389 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2003045912 | A1 | 20030605 | WO 2002-IB4757 | | 20021114 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| US 20030162787 | A1 | 20030828 | US 2002-278643 | | 20021023 |
| US 7030141 | B2 | 20060418 | | | |
| CA 2468715 | A1 | 20030605 | CA 2002-2468715 | | 20021114 |
| AU 2002365313 | A1 | 20030610 | AU 2002-365313 | | 20021114 |
| AU 2002365313 | B2 | 20080306 | | | |
| BR 2002014519 | A | 20041013 | BR 2002-14519 | | 20021114 |
| EP 1465864 | A1 | 20041013 | EP 2002-803885 | | 20021114 |
| EP 1465864 | B1 | 20060315 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | | |
| CN 1582274 | A | 20050216 | CN 2002-823837 | | 20021114 |
| HU 2004002529 | A2 | 20050329 | HU 2004-2529 | | 20021114 |
| JP 2005515985 | T | 20050602 | JP 2003-547364 | | 20021114 |
| AT 320414 | T | 20060415 | AT 2002-803885 | | 20021114 |
| EP 1671949 | A2 | 20060621 | EP 2006-110738 | | 20021114 |
| EP 1671949 | A3 | 20060719 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | | |
| PT 1465864 | T | 20060630 | PT 2002-803885 | | 20021114 |
| ES 2259113 | T3 | 20060916 | ES 2002-803885 | | 20021114 |
| NZ 532384 | A | 20061027 | NZ 2002-532384 | | 20021114 |
| AP 1744 | A | 20070630 | AP 2004-3035 | | 20021114 |
| MX 2004PA03606 | A | 20040727 | MX 2004-PA3606 | | 20040416 |
| ZA 2004004085 | A | 20050905 | ZA 2004-4085 | | 20040525 |
| NO 2004002270 | A | 20040601 | NO 2004-2270 | | 20040601 |
| US 20050267118 | A1 | 20051201 | US 2004-17598 | | 20041220 |
| US 20050250815 | A1 | 20051110 | US 2005-108582 | | 20050418 |
| US 20060264626 | A1 | 20061123 | US 2006-461859 | | 20060802 |
| PRIORITY APPLN. INFO.: | | | US 2001-334168P | P | 20011129 |

| | | |
|---|---|---|
| US 2002-384895P | P | 20020531 |
| US 2002-278643 | A3 | 20021023 |
| EP 2002-803885 | A3 | 20021114 |
| WO 2002-IB33416 | A | 20021114 |
| WO 2002-IB4757 | W | 20021114 |
| US 2004-17598 | A3 | 20041220 |

OTHER SOURCE(S): MARPAT 139:6763

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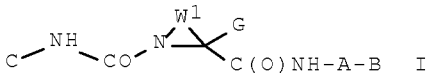



I

AB The present invention provides pyrrolidinedicarboxamides and related compds. (shown as I; variables defined below; e.g. (R)-pyrrolidine-1,2- dicarboxylic acid 1-[(4-chlorophenyl)amide] 2-[(3-fluoro-2'- sulfamoylbiphenyl-4-yl)amide]) and pharmaceutically acceptable salt thereof, that are useful to treat thrombotic disorders. Also disclosed are pharmaceutical compns. comprising ≥1 compds. I, processes for preparing I, and intermediates useful for preparing I. IC50 values for inhibition of factor Xa are tabulated for >170 examples of I. About 180 example prepns. of I are included. For example, (R)-pyrrolidine-1,2- dicarboxylic acid 1-[(4-chlorophenyl)amide] 2-[(3-fluoro-2'-sulfamoylbiphenyl-4-yl)amide] was prepared in 4 steps starting from Fmoc-D-Pro, SOCl2, and 4-bromo-2-fluoroaniline and involving intermediates (R)-2-[(4-bromo-2-fluorophenyl)carbamoyl]pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester, (R)-pyrrolidine-2-carboxylic acid (2'-tert-butylsulfamoyl-3-fluorobiphenyl-4-yl)amide, and (R)-pyrrolidine-1,2-dicarboxylic acid 2-[(2'-tert-butylsulfamoyl-3- fluorobiphenyl-4-yl)amide] 1-[(4-chlorophenyl)amide] with yields of 99, 70, 66 and 76%, resp. Four pharmaceutical formulations are described. For I: A is (un)substituted aryl or (un)substituted monocyclic heteroaryl; B is -NHC(O)(C1-C6)alkyl, -NHC(O)(C3-C7)cycloalkyl, -NHC(O)O(C1-C6 alkyl), -C(O)R1, (C3-C7)cycloalkyl, (C3-C7)heterocyclo, (C4-C7)cycloalkenyl, unsatd. (C4-C7)heterocyclo, aryl, or heteroaryl, any of which may be (un)substituted by halo, (C1-C6)alkyl, or halo(C1-C6)alkyl, O(C1-C6), -CN, haloalkyl, amino, alkylamino, amidino, amido, or sulfonamido. C is Ph or heteroaryl, wherein Ph or heteroaryl is (un)substituted with ≥1 substituents = aryl, heteroaryl, halogen, hydroxy, -CO2R2, -COR2, -CONR2R2', alkoxy, alkyl, -CN, haloalkyl, amino, alkylamino, amidino, amido, or sulfonamido; G is H, halo, (C1-C6)alkyl, halo(C1-C6)alkyl, hydroxy(C1-C6)alkyl, -CH2O(C1-C6)alkyl, -CH2CO2(C1-C6)alkyl, -CH2NR2R2', or -CH2C(O)NH(C1-C6)alkyl. W1 is a saturated or unsatd., (un)substituted hydrocarbon chain or hydrocarbon-heteroatom chain having 2-6 atoms, wherein W1 connects the N atom at position 1 to the C atom at position 2 to form a four to eight membered ring; R1 is (C1-C6)alkoxy, (C3-C7)cycloalkyl, (C3-C7)heterocycloalkyl, (C4-C7) cycloalkenyl, (C4-C7)heterocycloalkenyl, aryl, monocyclic heteroaryl, or -NR3R4; R2 and R2' are each independently H or (C1-C6)alkyl; and R3 and R4 are each independently H, (C1-C6)alkyl, aralkyl, aryl, monocyclic heteroaryl, alkoxycarbonyl, aralkoxycarbonyl, -SO2alkyl, or joined together to form a saturated or unsatd. 3 to 7 membered ring.

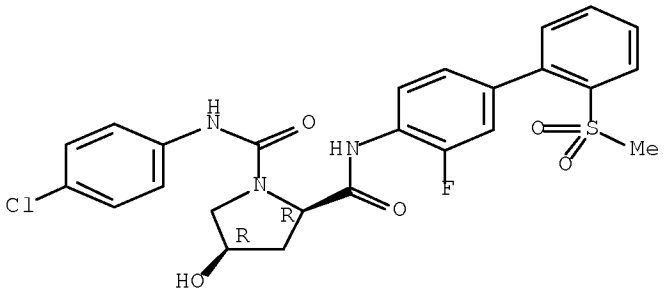
IT 536746-63-1P, (2R,4R)-4-Hydroxypyrrolidine-1,2-dicarboxylic acid 1-[(4-chlorophenyl)amide] 2-[(3-fluoro-2'-methanesulfonylbiphenyl-4-yl)amide]
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of pyrrolidinedicarboxamides and related compds. as inhibitors of factor Xa useful for thrombotic disorders)

RN 536746-63-1 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-N2-[3-fluoro-2'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]-4-hydroxy-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:352811 HCAPLUS Full-text

DOCUMENT NUMBER: 129:40984

ORIGINAL REFERENCE NO.: 129:8615a,8618a

TITLE: Preparation of acylamino-substituted acylanilide derivatives as antiandrogenic agents

INVENTOR(S): Taniguchi, Nobuaki; Okada, Minoru; Kaku, Hidetaka; Shimada, Itsuro; Nozawa, Eisuke; Koutoku, Hiroshi; et al.

PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9822432 | A1 | 19980528 | WO 1997-JP4174 | 19971117 |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9749664 | A | 19980610 | AU 1997-49664 | 19971117 |
| PRIORITY APPLN. INFO.: | | | JP 1996-306192 A | 19961118 |
| | | | WO 1997-JP4174 W | 19971117 |

OTHER SOURCE(S): MARPAT 129:40984

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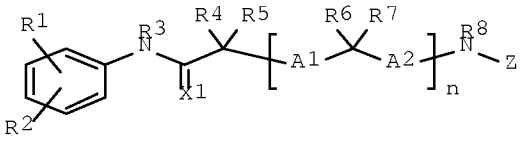


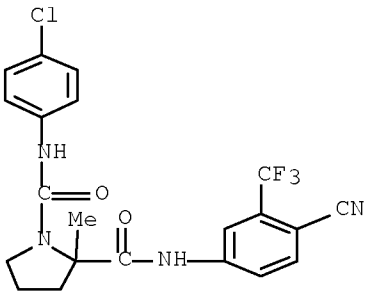
I

AB The title compds. [I; R1, R2 = halo, cyano, haloalkyl, NO2, etc.; R3 = H, lower alkyl; R4-R7 = H, (un)substituted lower alkyl, aralkyl, etc.; R8 = H, OH, lower alkoxy or alkyl, etc.; n = 0, 1; A1, A2 = lower alkylene; Z = acyl; X1 = O, S] are prepared I have an antiandrogenic activity and are useful as a prophylactic or therapeutic agent for prostatic cancer, prostatic hypertrophy, defemination, hypertrichosis, bald head, acne, seborrhea and the like in which androgen is involved as an exacerbating factor. Thus, p-FC6H4SO2NHCHEtCO2H was treated with (COCl)2 and then reacted with 4-amino-2-trifluoromethylbenzonitrile to give I (R1 = CF3, R2 = cyano, R3 = R5 = R8 = H, n = 0, Z = p-FC6H4SO2, X1 = O), which showed IC50 of 0.56 nM antagonist activity when tested with androgen receptor.

IT 208121-51-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acylamino-substituted acylanilide derivs. as antiandrogenic agents)

RN 208121-51-1 HCAPLUS

CN 1,2-Pyrrolidinedicarboxamide, N1-(4-chlorophenyl)-N2-[4-cyano-3-(trifluoromethyl)phenyl]-2-methyl- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 JUN 2008 HIGHEST RN 1028750-52-8
DICTIONARY FILE UPDATES: 17 JUN 2008 HIGHEST RN 1028750-52-8

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

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http://www.cas.org/support/stngen/stndoc/properties.html

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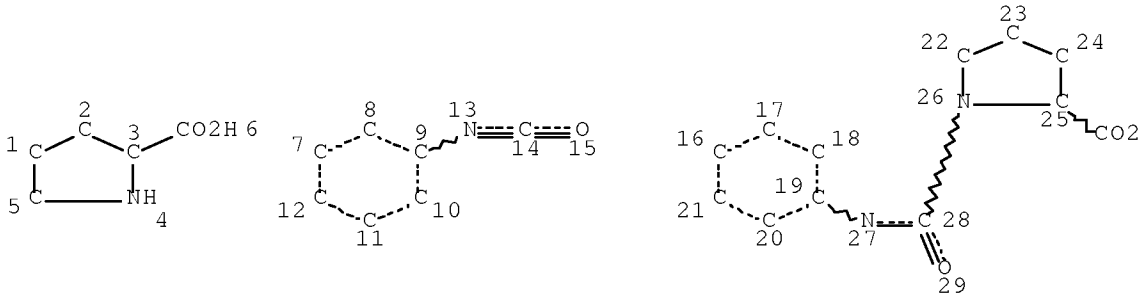

Page 1-A

H 30

Page 1-B
NODE ATTRIBUTES:
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE
L13 5 SEA FILE=CASREACT SSS FUL L11 ( 10 REACTIONS)

100.0% DONE 117 VERIFIED 10 HIT RXNS 5 DOCS
SEARCH TIME: 00.00.01

L13 ANSWER 1 OF 5 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 143:7713 CASREACT Full-text
TITLE: Preparation of spiro-heterocyclic compounds for treating inflammatory diseases and immune diseases
INVENTOR(S): Dhar, T. G. Murali; Iwanowicz, Edwin; Launay, Michele; Potin, Dominique; Blandine, Maillet Magali Jeannine; Nicolai, Eric
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Cerep SA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

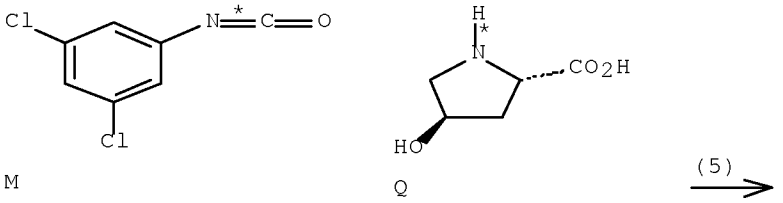
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 20050119279 | A1 | 20050602 | US 2004-957255 | 20041001 |
| US 7199125 | B2 | 20070403 | | |
| PRIORITY APPLN. INFO.: | | | US 2003-508165P | 20031002 |

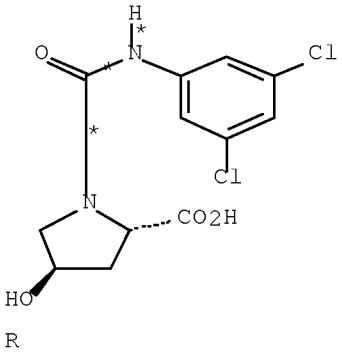
OTHER SOURCE(S): MARPAT 143:7713
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is directed to compds. having the formula (I) [K, L = O, S; Q = a bond, CO, (un)substituted branched or straight chain C1-6 alkylene; Ar = aryl, heteroaryl; Y = a bond, (un)substituted CH2; J1, J2, J3 = each (un)substituted NH or CH2; provided that only one of J1, J2, and J3 may be (un)substituted NH, so that ring A is a five- to six- membered cycloalkyl or heterocycle ring having from 0 to 2 heteroatoms; R1 = N, (un)substituted CH; R2, R3 = H, halo, NO2, cyano, (un)substituted alkyl or alkenyl, SR12, OR12, NR12R13, CO2R12, COR12, CONR12R13, aryl, heterocyclyl, cycloalkyl, heteroaryl; wherein R12, R13 = hydrogen, (un)substituted alkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl; or R12 and R13 when attached to the same nitrogen atom may be taken together to form a heteroaryl or heterocyclyl ring], stereoisomers, pharmaceutically acceptable salts, or hydrates, or prodrug thereof. These compds. are inhibitors of leukointegrins [integrins CD11/CD18, namely lymphocyte function-associated antigen 1 (LFA-1) and macrophage antigen 1 (Mac-1)] and intercellular adhesion mols. (ICAMs such as ICAM-1, ICAM-2, and ICAM-3) (no data). They are useful for treating LFA-1/ICAM-associated conditions, in particular inflammatory and immune diseases. Thus, to a solution of (7aS)-7a-[(4-bromophenyl)methyl]-2-(3,5-dichlorophenyl)dihydro-1H-pyrrolo[1,2-c]imidazole-1,3,6(2H,5H)-trione (0.12 g, 0.26 mmol) and (S)-lactamide (0.114 g, 1.3 mmol) in xylene (20 mL) was added p-toluenesulfonic acid (10 mg) and the resulting mixture was refluxed with the azeotropic removal of water for 18 h to give, after workup and silica gel chromatog., 1'H,4H-spiro(1,3-oxazolidine-2,6'-pyrrolo[1,2-c]imidazole)- 1',3',4(2'H)-trione (II) and (III).

RX(5) OF 97 M + Q ===> R...




RX(5) RCT M 34893-92-0, Q 51-35-4
RGT O 584-08-7 K2CO3
PRO R 433289-45-3
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) overnight, room temperature
NTE incremental addition of the reagent
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

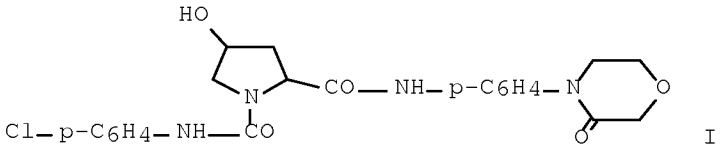
L13 ANSWER 2 OF 5 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 141:314626 CASREACT Full-text
TITLE: Method for the production of pyrrolidine-1,2-dicarboxylic acid-1-(phenyl(-amide))-2-(phenyl(-amide)) derivatives and 1-(phenylcarbamoyl)-pyrrolidine-2-carboxylic acid derivatives as intermediate products
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

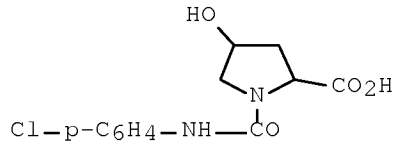
| | | | | |
|---|---|---|---|---|
| WO 2004087695 | A1 | 20041014 | WO 2004-EP2405 | 20040309 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| DE 10327428 | A1 | 20050105 | DE 2003-10327428 | 20030618 |
| DE 10329295 | A1 | 20050203 | DE 2003-10329295 | 20030630 |
| DE 10329457 | A1 | 20050120 | DE 2003-10329457 | 20030701 |
| DE 10334174 | A1 | 20050217 | DE 2003-10334174 | 20030726 |
| AU 2004226280 | A1 | 20041014 | AU 2004-226280 | 20040309 |
| CA 2520893 | A1 | 20041014 | CA 2004-2520893 | 20040309 |
| EP 1608646 | A1 | 20051228 | EP 2004-718646 | 20040309 |
| EP 1608646 | B1 | 20070711 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004008888 | A | 20060411 | BR 2004-8888 | 20040309 |
| JP 2006522037 | T | 20060928 | JP 2006-504602 | 20040309 |
| EP 1760081 | A1 | 20070307 | EP 2006-22891 | 20040309 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LT, LV | | | | |
| US 20060211692 | A1 | 20060921 | US 2005-551670 | 20050930 |
| IN 2005KN02182 | A | 20060929 | IN 2005-KN2182 | 20051103 |
| PRIORITY APPLN. INFO.: | | | DE 2003-10315377 | 20030403 |
| | | | DE 2003-10327428 | 20030618 |
| | | | DE 2003-10329295 | 20030630 |
| | | | DE 2003-10329457 | 20030701 |
| | | | DE 2003-10334174 | 20030726 |
| | | | EP 2004-718646 | 20040309 |
| | | | WO 2004-EP2405 | 20040309 |

OTHER SOURCE(S): MARPAT 141:314626

GI



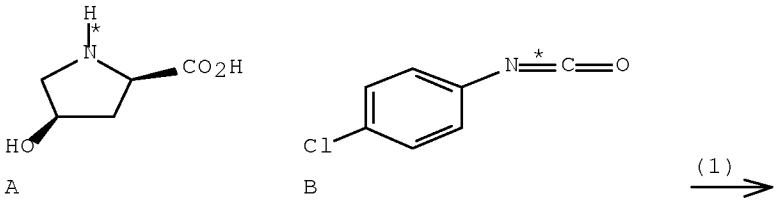

I



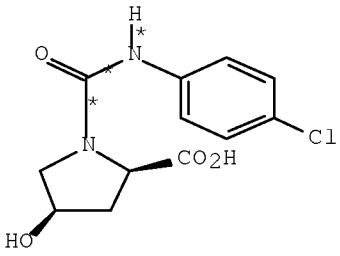

II

AB The invention relates to a method for the production of title compds., e.g. (I), and intermediate products, e.g. (II) for the production of I. Thus, cis-hydroxy-D-proline was reacted with 4-chlorophenylisocyante in NaHCO3 at 80° for 5 h. to give after workup 81.8% (R,R)-II. II was then reacted with 4-(3-oxo-4-morpholinyl)aniline in THF with 2-ethoxy-1(2H)-quinolinecarboxylic acid Et ester (EEDQ) as coupling agent at room temperature for 20 h to give, after workup, 69% (R,R)-I.

RX(1) OF 4 A + B ===> C...



A B (1)



C
YIELD 82%

RX(1) RCT A 2584-71-6, B 104-12-1

STAGE(1)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON SUBSTAGE(1) 5 hours, 80 deg C
SUBSTAGE(2) 80 deg C -> room temperature

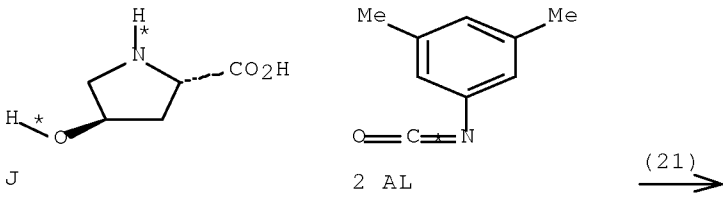
STAGE(2)
RGT E 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature, pH 1

PRO C 768370-72-5
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

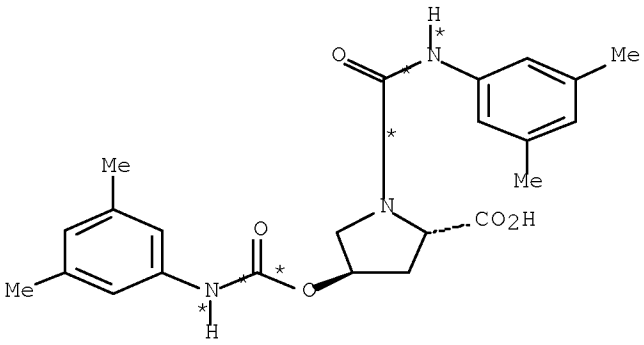
L13 ANSWER 3 OF 5 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 141:207487 CASREACT Full-text
TITLE: Synthetic studies on L-proline and (4R)-hydroxy-L-proline derivatives
AUTHOR(S): Gonzalez, Teresa; Abad, Olga; Santano, M. Carmen; Minguillon, Cristina
CORPORATE SOURCE: Laboratori de Quimica Farmaceutica, Facultat de Farmacia, Universitat de Barcelona, Barcelona, 08028, Spain
SOURCE: Synthesis (2004), (8), 1171-1182
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The preparation of a number of L-proline and (4R)-hydroxy-L-proline derivs. to assess their enantioselectivity when applied to several techniques and exptl. conditions is described. All the derivs. prepared via acylation of amino group in amino acid, followed by the reaction with appropriate amines incorporated at least one 3,5-disubstituted aromatic ring that contained nitro, chloro or Me groups and were obtained by classical methods. In spite of the difficulties that arise from the presence of rotational isomers in most cases, the compds. studied are fully described by their 1H and 13C NMR spectra.

RX(21) OF 75 J + 2 AL ===> AM




J 2 AL




AM
YIELD 78%

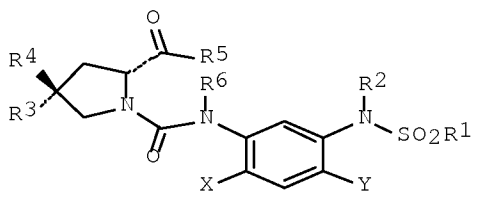
RX(21) RCT J 51-35-4, AL 54132-75-1

RGT AN 110-86-1 Pyridine
PRO AM 744253-81-4
CON 5 hours, reflux
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 5 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 129:202944 CASREACT Full-text
TITLE: Preparation of intermediates and 1,3-dioxo-1H-pyrrolo[1,2-c]imidazoles
INVENTOR(S): Taylor, Eric Deguyon; Petrov, Viacheslav Alexandrovich; Schaefer, Matthias; Drauz, Karlheinz; Vogt, Anne; Weckbecker, Christoph; Swearingen, Steven H.; Kamireddy, Balreddy
PATENT ASSIGNEE(S): E. I. Du Pont de Nemours & Co., USA; Degussa A.-G.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9837065 | A1 | 19980827 | WO 1998-US2721 | 19980213 |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| IN 1998CA00208 | A | 20051118 | IN 1998-CA208 | 19980209 |
| ZA 9801168 | A | 19990812 | ZA 1998-1168 | 19980212 |
| CA 2276056 | A1 | 19980827 | CA 1998-2276056 | 19980213 |
| AU 9861604 | A | 19980909 | AU 1998-61604 | 19980213 |
| EP 973739 | A1 | 20000126 | EP 1998-906363 | 19980213 |
| EP 973739 | B1 | 20051102 | | |
| R: DE, FR, IT | | | | |
| BR 9807256 | A | 20000502 | BR 1998-7256 | 19980213 |
| US 6384234 | B1 | 20020507 | US 1999-367899 | 19991230 |
| US 20020137946 | A1 | 20020926 | US 2002-35136 | 20020104 |
| US 6664400 | B2 | 20031216 | | |

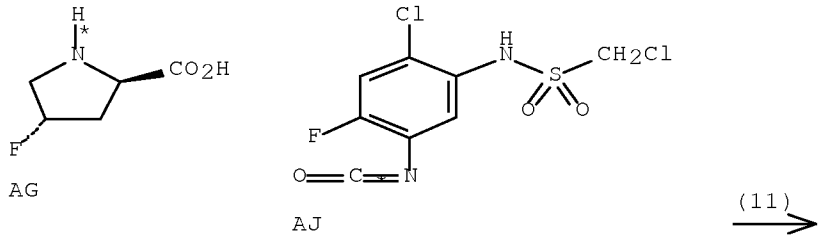
PRIORITY APPLN. INFO.: US 1997-38429P 19970219
WO 1998-US2721 19980213
US 1999-367899 19991230
OTHER SOURCE(S): MARPAT 129:202944
GI

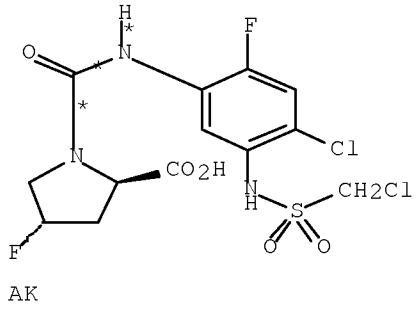



I

AB Title compds. [I; R1 = haloalkyl, alkoxyalkyl, cyanoalkyl, etc.; R2 = H, (halo)alkyl, alkanoyl, alkoxycarbonyl, etc.; R3 = H or OH; R4,X = H, F, Cl; Y = F or Cl; R5 = OH; R6 = H; R5R6 = bond] were prepared Thus, N-(2-chloro-4-fluoro-5-isocyanatophenyl)chloromethanesulfonamide (preparation given) was amidated by cis-4-hydroxy-D-proline to give I (R1 = Y = Cl, R2 = H, X = F)(II; R4 = R6 = H, R3 = R5 = OH) which was cyclized and the product fluorinated to give II (R3 = H, R4 = F, R5R6 = bond).

RX(11) OF 34 ..AG + AJ ===> AK




RX(11) RCT AG 131176-02-8, AJ 212198-49-7

STAGE(1)
SOL 109-99-9 THF

STAGE(2)
RGT AC 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt

STAGE(3)
RGT I 7647-01-0 HCl
SOL 7732-18-5 Water, 109-99-9 THF

PRO AK 212198-50-0

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

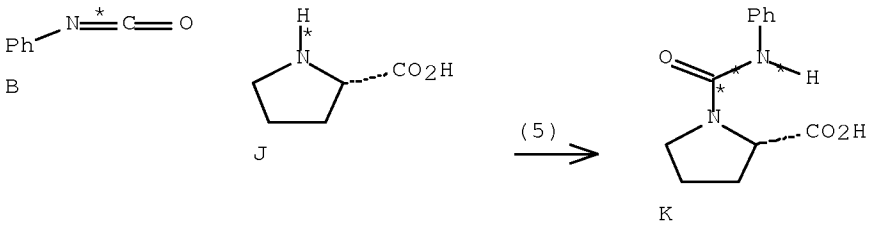
L13 ANSWER 5 OF 5 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 115:29919 CASREACT Full-text
TITLE: Process for preparation of unsymmetrical ureas and thioureas
INVENTOR(S): Henklein, Peter; Boettcher, Mathias; Georgi, Monika; Heder, Gottfried; Siems, Wolf Eberhard; Niedrich, Hartmut
PATENT ASSIGNEE(S): Akademie der Wissenschaften der DDR, Germany
SOURCE: Ger. (East), 3 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DD 285975 | A5 | 19910110 | DD 1985-294362 | 19851223 |

PRIORITY APPLN. INFO.: DD 1985-294362 19851223
OTHER SOURCE(S): MARPAT 115:29919

AB A process for the preparation of ureas R1NHCOR2 (R1 = aryl, alkyl; R2 = amino acid group, amino acid ester group) or thioureas R1NHCSR2 (same R1, R2) comprises the silylation of amino acid tosylates and subsequent treatment of the products with isocyanate or isothiocyanate. The sequential treatment of amino acid ester hydrochlorides with COCl2 and amino acid esters gives R1NHCOR2 (same R1, R2). Unsym. ureas or thioureas are potential inhibitors for angiotensin-converting enzyme which represents an approach to the treatment of renal hypertension. Isoleucine tosylate was silylated with hexamethyldisilazane and treated with PhNCO to give PhNHCONH(CO2H)CHMeEt (I). The IC50 of I for in vitro inhibition of angiotensin-converting enzyme was 70 μM. The IC50 of PhNHC(:S)NH(CO2H)CHMeEt was 165 μM.

RX(5) OF 6 B + J ===> K




RX(5) RCT B 103-71-9, J 147-85-3
PRO K 73096-22-7

=> fil medl,biosis,embase,hcaplus;s mederski w?/au;s tsaklakidis c?/au;s dorsch d?/au;s cezanne b?/au;s gleitz j?/au

FILE 'MEDLINE' ENTERED AT 15:45:51 ON 18 JUN 2008

FILE 'BIOSIS' ENTERED AT 15:45:51 ON 18 JUN 2008


FILE 'EMBASE' ENTERED AT 15:45:51 ON 18 JUN 2008


FILE 'HCAPLUS' ENTERED AT 15:45:51 ON 18 JUN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


L14 9 FILE MEDLINE
L15 43 FILE BIOSIS
L16 21 FILE EMBASE
L17 144 FILE HCAPLUS

TOTAL FOR ALL FILES
L18 217 MEDERSKI W?/AU

L19 2 FILE MEDLINE
L20 17 FILE BIOSIS
L21 2 FILE EMBASE
L22 78 FILE HCAPLUS

TOTAL FOR ALL FILES
L23 99 TSAKLAKIDIS C?/AU

L24 11 FILE MEDLINE
L25 47 FILE BIOSIS
L26 16 FILE EMBASE
L27 185 FILE HCAPLUS

TOTAL FOR ALL FILES
L28 259 DORSCH D?/AU

L29 4 FILE MEDLINE
L30 10 FILE BIOSIS
L31 4 FILE EMBASE
L32 48 FILE HCAPLUS

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L33 66 CEZANNE B?/AU

L34 26 FILE MEDLINE
L35 39 FILE BIOSIS
L36 31 FILE EMBASE
L37 83 FILE HCAPLUS

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L40 6 FILE BIOSIS

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PROCESSING COMPLETED FOR L43
L44          38 DUP REM L43 (6 DUPLICATES REMOVED)

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L44  ANSWER 1 OF 38  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
ACCESSION NUMBER:   2008:250260  BIOSIS  Full-text
DOCUMENT NUMBER:    PREV200800265066
TITLE:              Phenyl derivatives.
AUTHOR(S):          Anonymous; Dorsch, Dieter [Inventor];
                    Mederski, Werner [Inventor]; Tsaklakidis,
                    Christos [Inventor]; Cezanne, Bertram
                    [Inventor]; Gleitz, Johannes [Inventor]; Barnes,
                    Christopher [Inventor]
CORPORATE SOURCE:   Ober Ramstadt, Germany
                    ASSIGNEE: Merck Patent GmbH
PATENT INFORMATION: US 07273867 20070925
SOURCE:             Official Gazette of the United States Patent and Trademark
                    Office Patents, (SEP 25 2007)
                    CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE:      Patent
LANGUAGE:           English
ENTRY DATE:         Entered STN: 9 Apr 2008
                    Last Updated on STN: 9 Apr 2008
AB    Novel compounds of the formula I in which W, X, Y, T, R(1 )and R(2 )are as
      defined in Patent claim 1, are inhibitors of coagulation factor Xa and can be
      employed for the prophylaxis and/or therapy of thromboembolic disorders


L44  ANSWER 2 OF 38  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
ACCESSION NUMBER:   2007:280692  BIOSIS  Full-text
DOCUMENT NUMBER:    PREV200700267680
TITLE:              Derivatives of phenoxy-n-' 4-(isothiazolindin-1,
                    1-dioxid-2yl)phenyll-valerian-acid amide and other
                    compounds as inhibitors of the coagulation factor xa in the
                    treatment of thromboembolic diseases and tumors.
AUTHOR(S):          Anonymous; Dorsch, Dieter [Inventor];
                    Cezanne, Bertram [Inventor]; Tsaklakidis,
                    Christos [Inventor]; Mederski, Werner
                    [Inventor]; Gleitz, Johannes [Inventor]; Barnes,
                    Christopher [Inventor]
CORPORATE SOURCE:   Ober Ramstadt, Germany
                    ASSIGNEE: Merck Patent Gesellschaft
PATENT INFORMATION: US 07199133 20070403
SOURCE:             Official Gazette of the United States Patent and Trademark
                    Office Patents, (APR 3 2007)
                    CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE:      Patent
LANGUAGE:           English
ENTRY DATE:         Entered STN: 25 Apr 2007
                    Last Updated on STN: 25 Apr 2007
AB    Novel compounds of formula (I), wherein D, W, X, Y, T and R(1 )have the
      meanings cited in claim 1, are inhibitors of coagulation factor Xa and can be
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used for the prophylaxis and/or therapy of thromboembolic diseases and in the treatment of tumors

L44 ANSWER 3 OF 38 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:194788 BIOSIS Full-text
DOCUMENT NUMBER: PREV200700192695
TITLE: Carboxylic acid amides.
AUTHOR(S): Anonymous; Dorsch, Dieter [Inventor]; Mederski, Werner [Inventor]; Gleitz, Johannes [Inventor]; Cezanne, Bertram [Inventor]; Tsaklakidis, Christos [Inventor]; Barnes, Christopher [Inventor]
CORPORATE SOURCE: Ober Ramstadt, Germany
ASSIGNEE: Merck Patent GmbH
PATENT INFORMATION: US 07183277 20070227
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (FEB 27 2007)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Mar 2007
Last Updated on STN: 14 Mar 2007

AB Novel compounds of the formula I in which D, W, X, Y, T and R(1 )are as defined in Patent Claim 1, are inhibitors of coagulation factor Xa and can be employed for the prophylaxis and/or therapy of thromboembolic diseases and for the treatment of tumours.

L44 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:318582 HCAPLUS Full-text
DOCUMENT NUMBER: 144:350972
TITLE: Proline derivatives
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006034789 | A1 | 20060406 | WO 2005-EP10025 | 20050916 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| DE 102004047255 | A1 | 20060413 | DE 2004-102004047255 | 20040929 |

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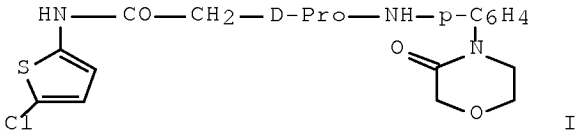
|---|---|---|---|---|
| AU 2005289184 | A1 | 20060406 | AU 2005-289184 | 20050916 |
| CA 2581737 | A1 | 20060406 | CA 2005-2581737 | 20050916 |
| EP 1797079 | A1 | 20070620 | EP 2005-787227 | 20050916 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 101031566 | A | 20070905 | CN 2005-80032791 | 20050916 |
| JP 2008514656 | T | 20080508 | JP 2007-533902 | 20050916 |
| MX 200703472 | A | 20070510 | MX 2007-3472 | 20070323 |
| KR 2007058543 | A | 20070608 | KR 2007-707056 | 20070328 |
| US 20070265259 | A1 | 20071115 | US 2007-576226 | 20070328 |
| IN 2007KN01475 | A | 20070720 | IN 2007-KN1475 | 20070425 |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004047255A | 20040929 |
| | | | WO 2005-EP10025 W | 20050916 |

OTHER SOURCE(S): MARPAT 144:350972

GI




I

AB The invention relates to title compds., e.g. (I), which are claimed as inhibitors of the coagulation factor Xa and can be used for the prophylaxis and/or therapy of thromboembolic diseases and for the treatment of tumors (no data). Thus, 4-(4-aminophenyl)morpholin-3-one (II) was condensed with Boc-D-Pro-OH; the resulting intermediate was then coupled with 2-chloro-N-(5-chlorothiophen-2-yl)acetamide to give I. Schemes depicting synthesis of several alternate II starting materials are given (no data), and thirteen alternate I compds. are claimed; formulations for use as injectable forms, suppositories, salves, tablets, dragees, capsules, or ampuls are given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:316811 HCAPLUS Full-text

DOCUMENT NUMBER: 144:370085

TITLE: Preparation of 1,2-pyrrolidinedicarboxamides as coagulation factor Xa inhibitors

INVENTOR(S): Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006034769 | A1 | 20060406 | WO 2005-EP9418 | 20050901 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, | | | | |

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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|---|---|---|---|---|
| DE 102004047254 | A1 | 20060413 | DE 2004-102004047254 | 20040929 |
| AU 2005289164 | A1 | 20060406 | AU 2005-289164 | 20050901 |
| CA 2581732 | A1 | 20060406 | CA 2005-2581732 | 20050901 |
| EP 1797071 | A1 | 20070620 | EP 2005-790356 | 20050901 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN 101031561 | A | 20070905 | CN 2005-80032789 | 20050901 |
| JP 2008514655 | T | 20080508 | JP 2007-533891 | 20050901 |
| MX 200703470 | A | 20070510 | MX 2007-3470 | 20070323 |
| KR 2007057878 | A | 20070607 | KR 2007-707053 | 20070328 |
| US 20080081814 | A1 | 20080403 | US 2007-576207 | 20070328 |
| IN 2007KN01474 | A | 20070720 | IN 2007-KN1474 | 20070425 |

PRIORITY APPLN. INFO.: DE 2004-102004047254A 20040929
WO 2005-EP9418 W 20050901

OTHER SOURCE(S): MARPAT 144:370085
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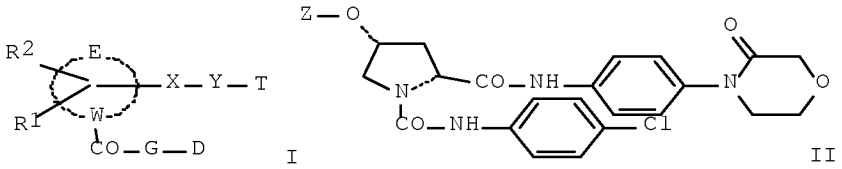



I II

AB Title compds. I [R1, R2 = H, =O, halo, etc.; R3 = H, CH2CH(OH)CH2OH, CH2CH(OH)CH2NH2, etc.; W = N, CR3 with provisos, etc.; E = together with W form a 3 to 7-membered hetero or carbocyclic ring with provisos; D = bond, double bond, etc.; G = [C(R4)2]n, [C(R4)2]nNR3, [C(R4)2]nO, etc.; R4 = H, A; A =alkyl with provisos; X = [C(R4)2]nCONR3[C(R4)2]n, etc.; n = 0-2; Y = alkylene, cycloalkylene, etc.; T = bond, double bond, heterocycle with provisos, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, O-acylation of hydroxypyrrolidine II [Z = H] afforded pyrrolidinedicarboxamide II [Z = CO2Et]. In coagulation factor Xa inhibition assays, pyrrolidinedicarboxamide II [Z = CO2Et] exhibited an IC50 value of 2.0x10-9 M.

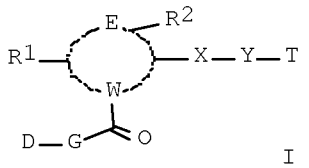
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:273940 HCAPLUS Full-text
DOCUMENT NUMBER: 144:331461
TITLE: Drugs containing carbonyl compounds and their use for the prophylaxis and/or therapy of thromboembolic illnesses
INVENTOR(S): Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner; Tsaklakidis,

Christos; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Ger. Offen., 77 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 102004045796 | A1 | 20060323 | DE 2004-102004045796 | 20040922 |
| AU 2005287637 | A1 | 20060330 | AU 2005-287637 | 20050824 |
| CA 2581172 | A1 | 20060330 | CA 2005-2581172 | 20050824 |
| WO 2006032342 | A2 | 20060330 | WO 2005-EP9124 | 20050824 |
| WO 2006032342 | A3 | 20070111 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| EP 1791597 | A2 | 20070606 | EP 2005-774750 | 20050824 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU | | | | |
| CN 101102818 | A | 20080109 | CN 2005-80031723 | 20050824 |
| JP 2008513387 | T | 20080501 | JP 2007-531628 | 20050824 |
| MX 200703175 | A | 20070518 | MX 2007-3175 | 20070316 |
| KR 2007054210 | A | 20070528 | KR 2007-706440 | 20070321 |
| US 20080003214 | A1 | 20080103 | US 2007-575711 | 20070321 |
| IN 2007KN01362 | A | 20070720 | IN 2007-KN1362 | 20070418 |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004045796A | 20040922 |
| | | | WO 2005-EP9124 W | 20050824 |

OTHER SOURCE(S): MARPAT 144:331461
GI



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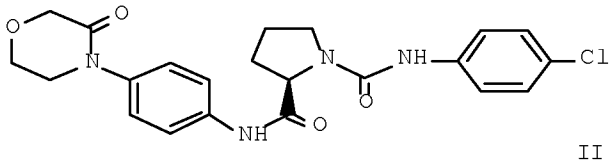

II

AB Use of heterocyclic carbonyl compds. I [R1, R2 = H, :O,,halogen, A, C.tplbond.CH, OR3,N(R3)2, NO2, CN, N3, CO2R3, CON(R3)2, [C(R4)2]n-Ar, [C(R4)2]n-heterocyclyl, [C(R4)2]n-cycloalkyl, OC(:O)R3, OC(:O)N(R3)2, NR3COA, NR3SO2A; R1R2 = bi- or spirocyclic 3- to 7-membered carbocycle or heterocycle (containing 0 - 3 N, O, or S); R3 = H, A, CH2C.tplbond.CH, CH2CH(OH)CH2OH, CH2CH(OH)CH2NH2, CH2CH(OH)CH2-heterocycle, [C(R4)2]n-Ar, [C(R4)2]n-heterocyclyl, [C(R4)2]n-cycloalkyl, [C(R4)2]n-CO2A, [C(R4)2]nN(R4)2; R4 = H, A; EW = 3- to 7-membered carbocycle or heterocycle (containing 0 - 3 N, O, or S); W = N, CR3, sp2-C; D = mono- or binuclear, (un)substituted aromatic carbocycle or heterocycle (containing 0 - 3 N, O, or S); G = [C(R4)2]n, [C(R4)2]n-NR3, [C(R4)2]nO, [C(R4)2]nS, [CR4:CR4]n; X = [C(R4)2]nCONR3[C(R4)2]n, [C(R4)2]nNR3CO[C(R4)2]n, [C(R4)2]nNR3[C(R4)2]n, [C(R4)2]nO[C(R4)2]n, [C(R4)2]nC(:O)[C(R4)2]n, [C(R4)2]nCO2[C(R4)2]n; Y = alkylene, cycloalkylene, heterodiyl, aryldiyl; T = mono- or binuclear, (un)substituted aromatic carbocycle or heterocycle (containing 0 - 3 N, O, or S); A = (un)branched C1-10-alkyl (optionally containing, O, S or CH:CH in the chain and replacing 1 - 7 H with F); n = 0 - 2; o = 1 - 3], their derivs., solvates, salts and stereoisomers, for the prophylaxis and/or therapy of thromboembolic illnesses. Thus, proline derivative II was prepared from N-Boc-D-proline via amidation with 4-(4-aminophenyl)morpholin-3-one in DMF containing 1-hydroxybenzotriazole hydrate, N-[3-(dimethylamino)propyl]-N'-ethylcarbodiimide hydrochloride and N-methylmorpholine, N-deprotection with aqueous HClin dioxane and carbamylation with 4-ClC6H4NCO in CH2Cl2 containing Et3N. The receptor binding activity of II was determined [IC50 = 1.8 x 10-8 M vs. FXa; IC50 = 2.3 x 10-8 M vs. TF/FVIIa].

L44 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1075769 HCAPLUS Full-text
DOCUMENT NUMBER: 143:347450
TITLE: Synthesis of prolinyl derivatives for use in the treatment of thromboembolic diseases or tumors
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005092849 | A1 | 20051006 | WO 2005-EP2306 | 20050304 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 102004014945 | A1 | 20051013 | DE 2004-102004014945 | 20040326 |
| AU 2005225489 | A1 | 20051006 | AU 2005-225489 | 20050304 |
| CA 2561057 | A1 | 20051006 | CA 2005-2561057 | 20050304 |
| EP 1735279 | A1 | 20061227 | EP 2005-715737 | 20050304 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LV | | | | |
| CN 1938269 | A | 20070328 | CN 2005-80009735 | 20050304 |
| BR 2005009174 | A | 20070918 | BR 2005-9174 | 20050304 |
| JP 2007530469 | T | 20071101 | JP 2007-504284 | 20050304 |
| IN 2006KN02397 | A | 20070525 | IN 2006-KN2397 | 20060824 |
| MX 2006PA10771 | A | 20061215 | MX 2006-PA10771 | 20060920 |
| KR 2007010131 | A | 20070122 | KR 2006-719772 | 20060925 |
| US 20070135507 | A1 | 20070614 | US 2006-594024 | 20060925 |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004014945A | 20040326 |
| | | | WO 2005-EP2306 W | 20050304 |

OTHER SOURCE(S): MARPAT 143:347450

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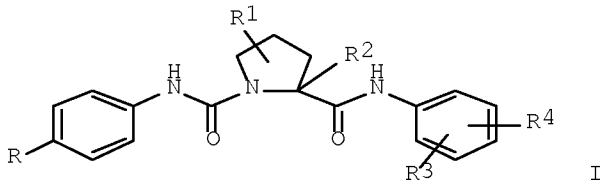


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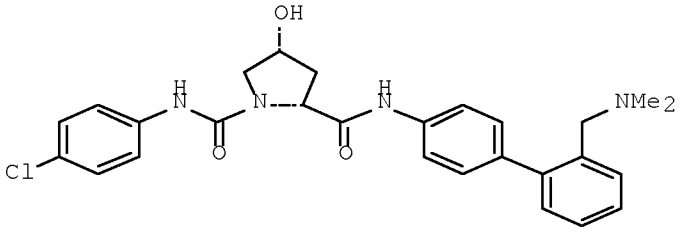


II

AB The invention relates to title compds., e.g. (I), which are inhibitors of coagulation factors Xa and VIIa and can be used for the prophylaxis and/or treatment of thromboembolic diseases and for the treatment of tumors (no data). Thus, (II) was prepared by condensation of (2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxylic acid 1-tert-Bu ester with 4'-amino-N,N-

dimethyl-[1,1'-biphenyl]-2-methanamine, followed by condensation with 4-nitrophenyl chloroformate and 4-chloroaniline, to give II (no yield). Sixteen title compds. are claimed, and formulations for administration (e.g., injections, suppositories, etc.) are given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:732627 HCAPLUS Full-text
DOCUMENT NUMBER: 143:211919
TITLE: Preparation of heterocyclic urea derivatives as coagulation factor Xa inhibitors.
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005073201 | A1 | 20050811 | WO 2005-EP83 | 20050107 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 102004004731 | A1 | 20050818 | DE 2004-102004004731 | 20040130 |
| AU 2005209362 | A1 | 20050811 | AU 2005-209362 | 20050107 |
| CA 2554911 | A1 | 20050811 | CA 2005-2554911 | 20050107 |
| EP 1709017 | A1 | 20061011 | EP 2005-700739 | 20050107 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| CN 1914184 | A | 20070214 | CN 2005-80003152 | 20050107 |
| BR 2005007165 | A | 20070626 | BR 2005-7165 | 20050107 |
| JP 2007519645 | T | 20070719 | JP 2006-549951 | 20050107 |
| IN 2006KN01699 | A | 20070511 | IN 2006-KN1699 | 20060620 |
| MX 2006PA08347 | A | 20060926 | MX 2006-PA8347 | 20060724 |
| US 20070161623 | A1 | 20070712 | US 2006-587855 | 20060728 |
| PRIORITY APPLN. INFO.: | | | DE 2004-102004004731A | 20040130 |
| | | | WO 2005-EP83 W | 20050107 |

OTHER SOURCE(S): CASREACT 143:211919; MARPAT 143:211919
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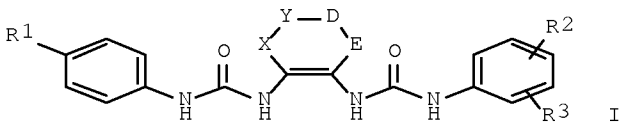


I

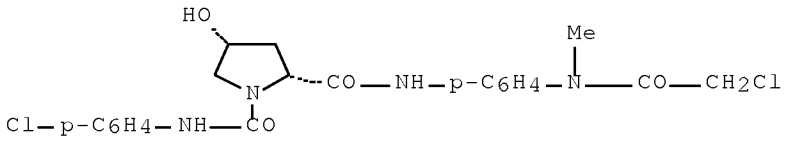
AB Title compds. [I; XYDE = (substituted) CH:CHCH:CH, N:CHCH:CH, N:CHN:CH, NHCOCH:CH, CH:CHN:CH, etc.; R1 = halo, C.tplbond.CH, C.tplbond.CA, OH, OA; R2 = H, halo, A; R3 = (substituted) 2-oxo-1H-pyridin-1-yl, 2-oxo-1H-pyrazin-1-yl, 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1-yl, 2-iminopiperidin-1-yl, 2-caprolactam-1-yl, etc.; A = (fluoro- and/or chloro-substituted) (cyclo)alkyl], were prepared Thus, 4-(4-amino-2- methylphenyl)morpholin-3-one in CH2Cl2 was treated with 4-nitrophenyl chloroformate and pyridine followed by stirring for 1 h. 1-(2-Amino-4-hydroxyphenyl)-3-(4-chlorophenyl)urethane (preparation given) and ethyldiisopropylamine were added followed by stirring for 20 h to give 18% 1-(4-chlorophenyl)-3-[4-hydroxy-2-[3-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]ureido]phenyl]urea. The latter showed FXa receptor affinity with IC500 = 12.0 nM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:564637 HCAPLUS Full-text
DOCUMENT NUMBER: 143:97636
TITLE: Synthesis of prolinylarylacetamides as coagulation factor Xa inhibitors for use in the prevention or treatment of thromboembolic diseases or tumors
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005058817 | A1 | 20050630 | WO 2004-EP13509 | 20041126 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10358814 | A1 | 20050721 | DE 2003-10358814 | 20031216 |
| AU 2004299197 | A1 | 20050630 | AU 2004-299197 | 20041126 |
| CA 2549589 | A1 | 20050630 | CA 2004-2549589 | 20041126 |
| EP 1697318 | A1 | 20060906 | EP 2004-820404 | 20041126 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| CN 1894210 | A | 20070110 | CN 2004-80037698 | 20041126 |
| BR 2004017630 | A | 20070327 | BR 2004-17630 | 20041126 |
| JP 2007513988 | T | 20070531 | JP 2006-544256 | 20041126 |
| IN 2006KN01579 | A | 20070504 | IN 2006-KN1579 | 20060608 |
| MX 2006PA06740 | A | 20060818 | MX 2006-PA6740 | 20060614 |

US 20070185189 A1 20070809 US 2006-583094 20060615
PRIORITY APPLN. INFO.: DE 2003-10358814 A 20031216
WO 2004-EP13509 W 20041126
OTHER SOURCE(S): MARPAT 143:97636
GI




I

AB Title compds., e.g. (I), are claimed as inhibitors of coagulation factor Xa and are claimed for use for the prophylaxis and/or therapy of thromboembolic diseases and in the treatment of tumors, as well as kits containing the compds. of interest. Thus, the title compds. were prepared, e.g., by condensation of (2R,4R)-1-(4-chlorophenylcarbamoyl)-4- hydroxyproline and N-(4-aminophenyl)2-dimethylamino-N-Me acetamide in DMF using N-(3-dimethylaminopropyl)-N'-ethyl-carbodiimide hydrochloride as condensing agent. In pharmacol. testing, I had receptor affinity IC50 values of 17.0 nM and 25.0 M using FXa and TF/FVIIa receptors, resp. (no details given). Various formulations for administering the title compds. therapeutically are given.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:540568 HCAPLUS Full-text
DOCUMENT NUMBER: 143:78086
TITLE: Preparation of urea/carbamate derivatives as inhibitors of coagulation factor Xa for treatment of thromoboembolic disorders
INVENTOR(S): Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005056528 | A1 | 20050623 | WO 2004-EP13202 | 20041119 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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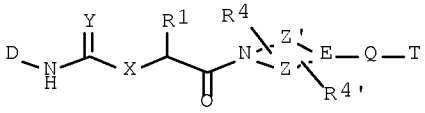
|---|---|---|---|---|
| DE 10358539 | A1 | 20050707 | DE 2003-10358539 | 20031215 |
| AU 2004296956 | A1 | 20050623 | AU 2004-296956 | 20041119 |
| CA 2549548 | A1 | 20050623 | CA 2004-2549548 | 20041119 |
| EP 1694643 | A1 | 20060830 | EP 2004-820053 | 20041119 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| CN 1890216 | A | 20070103 | CN 2004-80036500 | 20041119 |
| BR 2004017153 | A | 20070306 | BR 2004-17153 | 20041119 |
| JP 2007513987 | T | 20070531 | JP 2006-544246 | 20041119 |
| IN 2006KN01578 | A | 20070504 | IN 2006-KN1578 | 20060608 |
| MX 2006PA06593 | A | 20060731 | MX 2006-PA6593 | 20060609 |
| US 20070123509 | A1 | 20070531 | US 2006-582850 | 20060614 |

PRIORITY APPLN. INFO.: DE 2003-10358539 A 20031215
WO 2004-EP13202 W 20041119

OTHER SOURCE(S): CASREACT 143:78086; MARPAT 143:78086

GI



I

AB Title compds. I [D = halo, alkoxy, etc.; X = amino, O; Y = O, S, amino, etc.; R1 = H, aryl, heteroaryl, etc.; E = CH, N; Z, Z' = acyl, etc.; Q = O, amino, acyl, etc.; R4-4' = A, OH, alkoxy; T = (hetero)cyclyl, etc.] are prepared For instance, (R)-N-(4-chlorophenyl)-N'-[2-[4-(4- fluorophenyl)piperazin-1-yl]-2-oxo-1-phenylethyl]urea (II) is prepared in 3 steps from 1-methyl-4,4'-bipiperidinyl, (R)-N-(tert- butoxycarbonyl)phenylglycine and 4-chlorophenylisocyanate. II has IC50 = 6 x 10-9 M for Factor Xa. I are inhibitors of coagulation factor Xa and can be used for the prophylaxis and/or the treatment of thromboembolic diseases and for treating tumors.

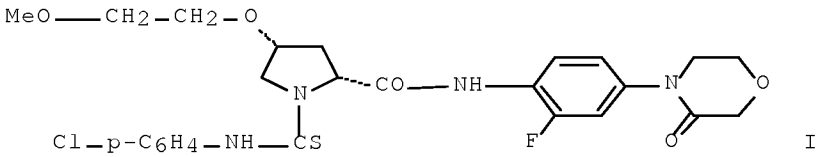
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1125507 HCAPLUS Full-text
DOCUMENT NUMBER: 143:387379
TITLE: Synthesis of thiocarbamoylproline derivatives for use as coagulation factor inhibitors in the prevention or treatment of thromboembolic diseases or tumors
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 102004016605 | A1 | 20051020 | DE 2004-102004016605 | 20040403 |
| WO 2005097783 | A1 | 20051020 | WO 2005-EP2745 | 20050315 |
| WO 2005097783 | A8 | 20070419 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA

PRIORITY APPLN. INFO.: DE 2004-102004016605A 20040403
OTHER SOURCE(S): MARPAT 143:387379
GI



I

AB Title compds., e.g. (I), their stereoisomeric forms and physiol. acceptable salts, are claimed for use as inhibitors of coagulation factor Xa or VIIa in the prevention or treatment of thromboembolic illnesses or tumors. Thus, I was prepared by reaction Boc-protected (2R,4R)-4-(2- methoxy)ethoxyproline with 4-(4-amino-3-fluorophenyl)-morpholin-3-one hydrochloride, treating the resulting product with 4N HCl to give the deprotected HCl salt, and condensing this with 4-chlorophenyl- isothiocyanate. In affinity tests with FXa and TF/FVIIa receptors (no details given), I had IC50 of 4.1 and 4.0 x 10-9, resp.

L44 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1124627 HCAPLUS Full-text
DOCUMENT NUMBER: 142:74838
TITLE: Preparation of pyrrolidin-1,2-dicarboxylic acids and related compounds as coagulation factor Xa and factor VIIa inhibitors
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cesanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004110433 | A1 | 20041223 | WO 2004-EP5717 | 20040527 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| DE 10327428 | A1 | 20050105 | DE 2003-10327428 | 20030618 |
| DE 10329457 | A1 | 20050120 | DE 2003-10329457 | 20030701 |
| AU 2004246766 | A1 | 20041223 | AU 2004-246766 | 20040527 |
| CA 2529453 | A1 | 20041223 | CA 2004-2529453 | 20040527 |
| EP 1633346 | A1 | 20060315 | EP 2004-735007 | 20040527 |
| EP 1633346 | B1 | 20060823 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

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|---|---|---|---|---|
| BR 2004011466 | A | 20060711 | BR 2004-11466 | 20040527 |
| CN 1809346 | A | 20060726 | CN 2004-80016955 | 20040527 |
| AT 337000 | T | 20060915 | AT 2004-735007 | 20040527 |
| JP 2006527708 | T | 20061207 | JP 2006-515798 | 20040527 |
| ES 2271894 | T3 | 20070416 | ES 2004-735007 | 20040527 |
| IN 2005KN02399 | A | 20070727 | IN 2005-KN2399 | 20051128 |
| MX 2005PA13536 | A | 20060309 | MX 2005-PA13536 | 20051213 |
| US 20070093472 | A1 | 20070426 | US 2005-561227 | 20051219 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 2003-10327428 | A | 20030618 |
| | DE 2003-10329457 | A | 20030701 |
| | WO 2004-EP5717 | W | 20040527 |

OTHER SOURCE(S): MARPAT 142:74838
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R = H, X, A, etc.; R1 = H, =O, halo, etc.; R2 = H, halo, A; R3 = (un)substituted aromatic heterocycle containing 1-4 N, O, S atoms; X = aryl, arylalkyl, het, etc.; A = (un)substituted cycloalkyl] and their pharmaceutically acceptable salts and formulations were prepared For example, condensation of proline II, e.g., prepared from BOC-methoxyproline in 3-steps, and 4-nitrophenylchloroformate and 4-ethynylaniline afforded claimed pyrrolidinyldicarboxylic III in 40% yield. In coagulation factor Xa receptor affinity binding assays, 14-examples of compds. I exhibited IC50 values ranging from 1.1-4.8 nM, i.e., the IC50 value of pyrrolidinyldicarboxylic III was 1.3 nM. Compds. I are claimed to be useful as factor Xa and factor VIIa inhibitors for the treatment of thromboembolic diseases.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1080898 HCAPLUS Full-text
DOCUMENT NUMBER: 142:56358
TITLE: Preparation of aroylsemicarbazides as factor Xa inhibitors for the treatment of thromboembolic diseases
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004108718 | A1 | 20041216 | WO 2004-EP5088 | 20040512 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10325962 | A1 | 20041223 | DE 2003-10325962 | 20030607 |
| AU 2004245187 | A1 | 20041216 | AU 2004-245187 | 20040512 |
| CA 2528233 | A1 | 20041216 | CA 2004-2528233 | 20040512 |
| EP 1633745 | A1 | 20060315 | EP 2004-732283 | 20040512 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004010617 | A | 20060620 | BR 2004-10617 | 20040512 |
| CN 1802370 | A | 20060712 | CN 2004-80015854 | 20040512 |
| JP 2006527217 | T | 20061130 | JP 2006-515768 | 20040512 |
| IN 2005KN02382 | A | 20061027 | IN 2005-KN2382 | 20051125 |
| MX 2005PA13035 | A | 20060302 | MX 2005-PA13035 | 20051202 |
| US 20060241111 | A1 | 20061026 | US 2006-559385 | 20060621 |

PRIORITY APPLN. INFO.: DE 2003-10325962 A 20030607
WO 2004-EP5088 W 20040512

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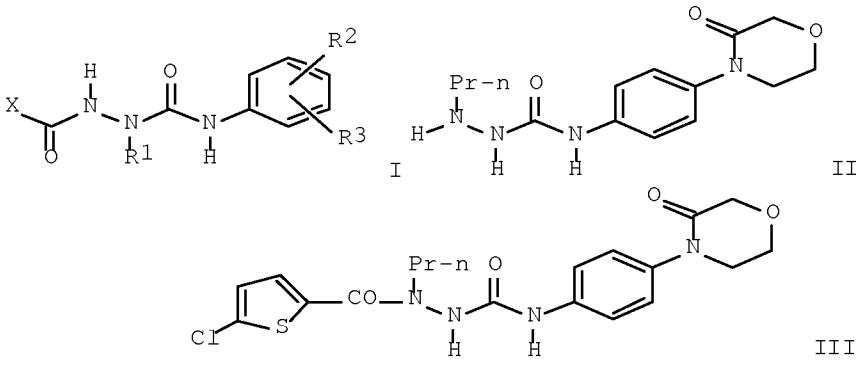


AB Title compds. I [X = Het; Het = bicyclic aromatic heterocycle with 1-3 N, O, or S atoms; R1 = A, S(O)mA, Ph, etc.; R2 = H, halo, A; A = H, (un)substituted cycloalkyl; R3 = 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1- yl, 2-oxo-1H-pyridin-1-yl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, coupling of amine II, i.e., prepared from 4-(4-aminophenyl)morpholin-3-one in 4-steps, and 5-chlorothiophen-2-carboxylic acid

afforded aroylsemicarbazide III in 51% yield. In coagulation factor Xa receptor affinity binding assays, 3-examples of compds. I exhibited IC50 values ranging from 87-390 nM, i.e., the IC50 value of aroylsemicarbazide III was 390 nM. Compds. I are claimed to be useful for the treatment of thromboembolic diseases.

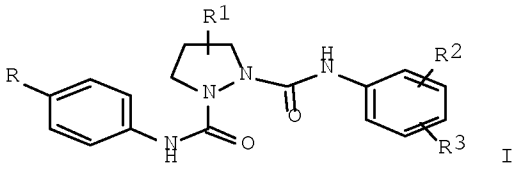
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:857592 HCAPLUS Full-text
DOCUMENT NUMBER: 141:332196
TITLE: Preparation of pyrazolidine-1,2-dicarboxamides as Factor Xa inhibitors for the treatment of thrombosis
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004087696 | A1 | 20041014 | WO 2004-EP2407 | 20040309 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| DE 10329295 | A1 | 20050203 | DE 2003-10329295 | 20030630 |
| DE 10336570 | A1 | 20050224 | DE 2003-10336570 | 20030808 |
| AU 2004226281 | A1 | 20041014 | AU 2004-226281 | 20040309 |
| CA 2520894 | A1 | 20041014 | CA 2004-2520894 | 20040309 |
| EP 1608645 | A1 | 20051228 | EP 2004-718641 | 20040309 |
| EP 1608645 | B1 | 20070502 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004008444 | A | 20060404 | BR 2004-8444 | 20040309 |
| JP 2006522038 | T | 20060928 | JP 2006-504604 | 20040309 |
| US 20060183742 | A1 | 20060817 | US 2005-551559 | 20051003 |
| IN 2005KN02183 | A | 20070323 | IN 2005-KN2183 | 20051103 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 2003-10315377 | A | 20030403 |
| | DE 2003-10329295 | A | 20030630 |
| | DE 2003-10336570 | A | 20030808 |
| | WO 2004-EP2407 | W | 20040309 |

OTHER SOURCE(S): MARPAT 141:332196
GI



I

AB Title compds. [I; R = H, A, ACO, halo, C.tplbond.CA, C.tplbond.CCOA; R1 = H, O, halo, OH, OA, ACO2, ACONH, ACONA, N3, NH2, NO2, CO2H, CO2A, CONH2, CONHA, allyloxy, propargyloxy, benzyloxy, :NOH, :CF2, etc.; R2 = H, halo, A; R3 = (unsatd.) (substituted) heterocyclyl; A = (fluoro and/or chloro-substituted) (cyclo)alkyl], were prepared Thus, pyrazolidine-1,2- dicarboxylic acid 1-[(4-ethynylphenyl)amide]-2-[[3-chloro-4-(3- oxomorpholin-4-yl)phenyl]amide] [preparation from 4-(4-amino-2- chlorophenyl)morpholin-3-one, tert-Bu pyrazolidine-1-carboxylate, and 4-ethynylaniline given] bound to Factor Xa receptors with IC50 = 75 nM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:857591 HCAPLUS Full-text
DOCUMENT NUMBER: 141:314626
TITLE: Method for the production of pyrrolidine-1,2-dicarboxylic acid-1-(phenyl(-amide))-2-(phenyl(-amide)) derivatives and 1-(phenylcarbamoyl)-pyrrolidine-2-carboxylic acid derivatives as intermediate products
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004087695 | A1 | 20041014 | WO 2004-EP2405 | 20040309 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| DE 10327428 | A1 | 20050105 | DE 2003-10327428 | 20030618 |
| DE 10329295 | A1 | 20050203 | DE 2003-10329295 | 20030630 |
| DE 10329457 | A1 | 20050120 | DE 2003-10329457 | 20030701 |

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| DE 10334174 | A1 | 20050217 | DE 2003-10334174 | 20030726 |
| AU 2004226280 | A1 | 20041014 | AU 2004-226280 | 20040309 |
| CA 2520893 | A1 | 20041014 | CA 2004-2520893 | 20040309 |
| EP 1608646 | A1 | 20051228 | EP 2004-718646 | 20040309 |
| EP 1608646 | B1 | 20070711 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004008888 | A | 20060411 | BR 2004-8888 | 20040309 |
| JP 2006522037 | T | 20060928 | JP 2006-504602 | 20040309 |
| EP 1760081 | A1 | 20070307 | EP 2006-22891 | 20040309 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LT, LV | | | | |
| US 20060211692 | A1 | 20060921 | US 2005-551670 | 20050930 |
| IN 2005KN02182 | A | 20060929 | IN 2005-KN2182 | 20051103 |

PRIORITY APPLN. INFO.:

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| DE 2003-10315377 | A | 20030403 |
| DE 2003-10327428 | A | 20030618 |
| DE 2003-10329295 | A | 20030630 |
| DE 2003-10329457 | A | 20030701 |
| DE 2003-10334174 | A | 20030726 |
| EP 2004-718646 | A3 | 20040309 |
| WO 2004-EP2405 | W | 20040309 |

OTHER SOURCE(S): CASREACT 141:314626; MARPAT 141:314626

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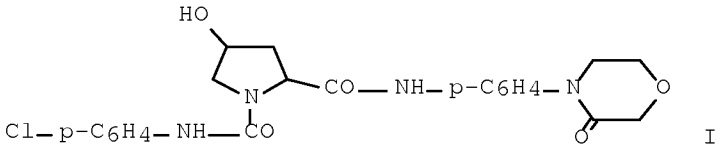


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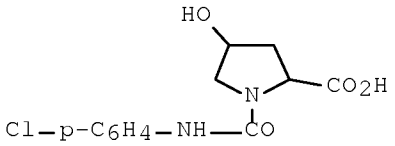


II

AB The invention relates to a method for the production of title compds., e.g. (I), and intermediate products, e.g. (II) for the production of I. Thus, cis-hydroxy-D-proline was reacted with 4-chlorophenylisocyante in NaHCO3 at 80° for 5 h. to give after workup 81.8% (R,R)-II. II was then reacted with 4-(3-oxo-4-morpholinyl)aniline in THF with 2-ethoxy-1(2H)-quinolinecarboxylic acid Et ester (EEDQ) as coupling agent at room temperature for 20 h to give, after workup, 69% (R,R)-I.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:857551 HCAPLUS Full-text

DOCUMENT NUMBER: 141:350179

TITLE: Preparation of azolidinedicarboxamides and related compounds as Factor Xa and Factor VIIa inhibitors

INVENTOR(S): Tsaklakidis, Christos; Dorsch, Dieter; Mederski, Werner; Cezanne,

Bertram; Gleitz, Johannes

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004087646 | A2 | 20041014 | WO 2004-EP2350 | 20040308 |
| WO 2004087646 | A3 | 20050106 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| DE 10329295 | A1 | 20050203 | DE 2003-10329295 | 20030630 |
| AU 2004226278 | A1 | 20041014 | AU 2004-226278 | 20040308 |
| CA 2521069 | A1 | 20041014 | CA 2004-2521069 | 20040308 |
| BR 2004008420 | A | 20060321 | BR 2004-8420 | 20040308 |
| JP 2006522033 | T | 20060928 | JP 2006-504581 | 20040308 |
| EP 1720844 | A2 | 20061115 | EP 2004-718299 | 20040308 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LT, LV | | | | |
| IN 2005KN01684 | A | 20070727 | IN 2005-KN1684 | 20050823 |
| US 20060183739 | A1 | 20060817 | US 2005-551557 | 20051003 |

PRIORITY APPLN. INFO.:
DE 2003-10315377 A 20030403
DE 2003-10329295 A 20030630
US 2003-483897P P 20030702
WO 2004-EP2350 W 20040308

OTHER SOURCE(S): MARPAT 141:350179

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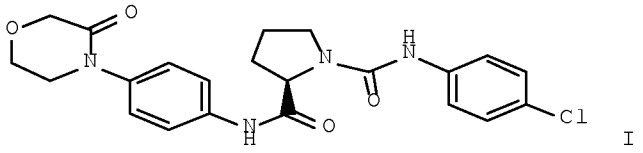

I

AB R1R2(TYX)EWCOGD [R1, R2 = H, O, halo, A, ethynyl, OR3, N(R3)2, NO2, cyano, N3, CO2R3, CON(R3)2, etc.; R3 = H, A, HC.tplbond.CCH2, MeC.tplbond.CCH2, CH2CH(OH)CH2OH, etc.; R4 = H, A; W = N, C, CR3; E = atoms to form a 3-7 membered (heterocyclic) ring optionally containing a double bond; D = mono- or dinuclear (substituted) (hetero)aryl; G = [C(R4)2]n, [C(R4)2]nNR3, [C(R4)2]nO, [C(R4)2]nS, etc.; n = 0-2; X = [C(R4)2]nCO[C(R4)2]n, [C(R4)2]n,NR3[C(R4)2]n,

[C(R4)2]nNR3CO[C(R4)2]n, etc.; Y = alkylene, cycloalkylene, heterocyclylene, arenediyl; T = substituted mono- or dinuclear carbocyclyl, heterocyclyl; A = (fluoro-substituted) alkyl optionally interrupted by O, S, CH:CH], were prepared Thus, title compound (I) [preparation from 4-(4-aminophenyl)morpholin-3-one, Boc-D-proline, and 4-chlorophenyl isocyanate given] bound to Factor Xa receptors with IC50 = 1.8 + 10-8 M.

L44 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:20490 HCAPLUS Full-text
DOCUMENT NUMBER: 140:77148
TITLE: Preparation of N-[4-(thiooxoheterocyclyl)phenyl]-2-phenyl-2H-pyrazole-3-carboxamides and corresponding imino-heterocyclyl derivatives as inhibitors of the coagulation factors Xa and/or VIIa for treating thrombosis
INVENTOR(S): Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004002477 | A1 | 20040108 | WO 2003-EP5898 | 20030605 |
| WO 2004002477 | A8 | 20040415 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10229070 | A1 | 20040115 | DE 2002-10229070 | 20020628 |
| CA 2491271 | A1 | 20040108 | CA 2003-2491271 | 20030605 |
| AU 2003238475 | A1 | 20040119 | AU 2003-238475 | 20030605 |
| EP 1517685 | A1 | 20050330 | EP 2003-732540 | 20030605 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005535630 | T | 20051124 | JP 2004-516575 | 20030605 |
| EP 1679073 | A1 | 20060712 | EP 2006-157 | 20030605 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | |
| US 20050203127 | A1 | 20050915 | US 2004-519356 | 20041228 |

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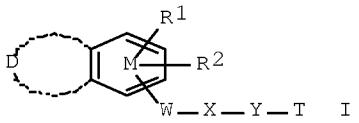
|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 2002-10229070 | A | 20020628 |
| | EP 2003-732540 | A3 | 20030605 |
| | WO 2003-EP5898 | W | 20030605 |

OTHER SOURCE(S): MARPAT 140:77148
GI



AB Title compds. [I; D = (N-, O-, S-interrupted) (substituted) C3-4 alkylene; M = Ph, aromatic heterocyclyl; R1, R2 = H, halo, (branched) (interrupted) (substituted) alkyl, NO2, cyano, OR3, N(R3)2, CO2R3, CON(R3)2, C(:S)N(R3)2, etc.; R3 = H, (branched) (interrupted) (substituted) alkyl, etc.; W = (substituted) (bi)cyclic aromatic (hetero)cyclyl; X = CONR3, CONR3C(R4)2, C(R4)2NR3, etc.; R4 = H, (branched) (interrupted) (substituted) alkyl; Y = alkylene, cycloalkylene, heterodiyl, aryldiyl; T = (substituted) (bi)cyclic aromatic heterocyclyl], were prepared Thus, 333 mg (3-[5-(4-[2-iminopyrrolidin-1-yl]phenylcarbamoyl)-3-trifluoromethylpyrazol- 1-yl]benzyl)carbamic acid tert-Bu ester (preparation given) in EtOH was treated with HCl in ether to give 289 mg N-[4-(2-iminopyrrolidin-1-yl)phenyl]-1-(3-aminomethylphenyl)-3-(trifluoromethyl)-1H-pyrazole-5-carboxamide. The latter gave affinity to the receptor Xa with IC50 = 9,6·10-9 M and to the receptor VIIa with IC50 = 2,3·10-8 M.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:841766 HCAPLUS Full-text
DOCUMENT NUMBER: 141:332202
TITLE: Preparation of azolidinecarboxamides as antithrombotics and anticancer drugs.
INVENTOR(S): Tsaklakidis, Christos; Dorsch, Dieter; Mederski, Werner; Cezanne, Bertram; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: Ger. Offen., 47 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10315377 | A1 | 20041014 | DE 2003-10315377 | 20030403 |
| AU 2004226278 | A1 | 20041014 | AU 2004-226278 | 20040308 |
| CA 2521069 | A1 | 20041014 | CA 2004-2521069 | 20040308 |
| WO 2004087646 | A2 | 20041014 | WO 2004-EP2350 | 20040308 |
| WO 2004087646 | A3 | 20050106 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2004008420 | A | 20060321 | BR 2004-8420 | 20040308 |

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|---|---|---|---|---|---|---|
| CN | 1771237 | A | 20060510 | CN | 2004-80009354 | 20040308 |
| JP | 2006522033 | T | 20060928 | JP | 2006-504581 | 20040308 |
| EP | 1720844 | A2 | 20061115 | EP | 2004-718299 | 20040308 |
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| AU | 2004226280 | A1 | 20041014 | AU | 2004-226280 | 20040309 |
| AU | 2004226281 | A1 | 20041014 | AU | 2004-226281 | 20040309 |
| CA | 2520893 | A1 | 20041014 | CA | 2004-2520893 | 20040309 |
| CA | 2520894 | A1 | 20041014 | CA | 2004-2520894 | 20040309 |
| WO | 2004087695 | A1 | 20041014 | WO | 2004-EP2405 | 20040309 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| WO | 2004087696 | A1 | 20041014 | WO | 2004-EP2407 | 20040309 |
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| EP | 1608645 | A1 | 20051228 | EP | 2004-718641 | 20040309 |
| EP | 1608645 | B1 | 20070502 | | | |
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| EP | 1608646 | A1 | 20051228 | EP | 2004-718646 | 20040309 |
| EP | 1608646 | B1 | 20070711 | | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | | |
| BR | 2004008444 | A | 20060404 | BR | 2004-8444 | 20040309 |
| BR | 2004008888 | A | 20060411 | BR | 2004-8888 | 20040309 |
| CN | 1771248 | A | 20060510 | CN | 2004-80009374 | 20040309 |
| CN | 1771249 | A | 20060510 | CN | 2004-80009463 | 20040309 |
| JP | 2006522037 | T | 20060928 | JP | 2006-504602 | 20040309 |
| JP | 2006522038 | T | 20060928 | JP | 2006-504604 | 20040309 |
| AT | 361296 | T | 20070515 | AT | 2004-718641 | 20040309 |
| AT | 366732 | T | 20070815 | AT | 2004-718646 | 20040309 |
| ES | 2285444 | T3 | 20071116 | ES | 2004-718641 | 20040309 |
| ES | 2287708 | T3 | 20071216 | ES | 2004-718646 | 20040309 |
| IN | 2005KN01684 | A | 20070727 | IN | 2005-KN1684 | 20050823 |
| US | 20060211692 | A1 | 20060921 | US | 2005-551670 | 20050930 |
| US | 20060183739 | A1 | 20060817 | US | 2005-551557 | 20051003 |
| US | 20060183742 | A1 | 20060817 | US | 2005-551559 | 20051003 |
| IN | 2005KN02182 | A | 20060929 | IN | 2005-KN2182 | 20051103 |
| IN | 2005KN02183 | A | 20070323 | IN | 2005-KN2183 | 20051103 |
| PRIORITY APPLN. INFO.: | | | | DE | 2003-10315377 A | 20030403 |
| | | | | DE | 2003-10327428 A | 20030618 |
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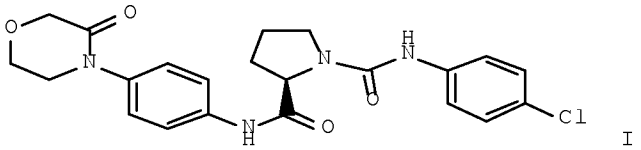
| DE 2003-10329457 | A | 20030701 |
| US 2003-483897P | P | 20030702 |
| DE 2003-10334174 | A | 20030726 |
| DE 2003-10336570 | A | 20030808 |
| WO 2004-EP2350 | W | 20040308 |
| WO 2004-EP2405 | W | 20040309 |
| WO 2004-EP2407 | W | 20040309 |

OTHER SOURCE(S): MARPAT 141:332202
GI



I

AB R1R2(TYX)EWCOGD [R1, R2 = H, O, halo, A, ethynyl, OR3, NO2, cyano, N3, CO2R3, CON(R3)2, NR3COA, NR3SO2A, etc.; R1R2 = toms to form a bicyclic or spirocyclic (heterocyclic) ring; R3 = H, A, etc.; R4 = H, A; W = N, CR3, C; E = atoms to form a 3-7 membered (double bond containing) (heterocyclic) ring with W; G = [C(R4)2]n, [C(R4)2]nNR3, [C(R4)2]nO, [C(R4)2]nS; X = [C(R4)2]nCONR3[C(R4)2]n, [C(R4)2]nON[C(R4)2]n, etc.; Y = alkylene, cycloalkylene, (substituted) heterocyclylene, arylene; T = mono- or bicyclic substituted (unsatd.) (hetero)cyclyl; A = (fluoro-substituted) alkylene optionally interrupted by O, S, CH:CH; n = 0-2], were prepared Thus, title compound (I) (prepared from 4-(4-aminophenyl)morpholin-3-one, Boc-D-proline, and 4-chlorophenyl isocyanate), bound to Factor Xa receptors with IC50 = 1.8 + 10-8 M.

L44 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:738402 HCAPLUS Full-text
DOCUMENT NUMBER: 141:243828
TITLE: Synthesis of amino acid ethylene derivatives for use as coagulation factor Xa inhibitors for treatment of disease
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Dorsch, Dieter; Cezanne, Bertram; Gleitz, Johannes; Van Amsterdam, Christoph
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10308907 | A1 | 20040909 | DE 2003-10308907 | 20030228 |
| AU 2004215708 | A1 | 20040910 | AU 2004-215708 | 20040130 |
| CA 2517391 | A1 | 20040910 | CA 2004-2517391 | 20040130 |
| WO 2004076429 | A1 | 20040910 | WO 2004-EP817 | 20040130 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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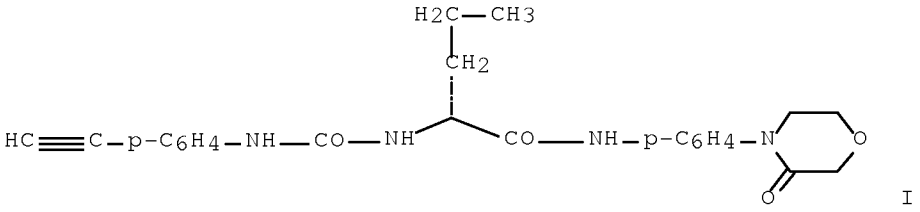
|---|---|---|---|---|
| EP 1597244 | A1 | 20051123 | EP 2004-706669 | 20040130 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2004007865 | A | 20060301 | BR 2004-7865 | 20040130 |
| CN 1753882 | A | 20060329 | CN 2004-80005443 | 20040130 |
| JP 2006519188 | T | 20060824 | JP 2006-501655 | 20040130 |
| MX 2005PA09002 | A | 20051018 | MX 2005-PA9002 | 20050824 |
| US 20060084648 | A1 | 20060420 | US 2005-547130 | 20050826 |
| PRIORITY APPLN. INFO.: | | | DE 2003-10308907 A | 20030228 |
| | | | WO 2004-EP817 W | 20040130 |

OTHER SOURCE(S): MARPAT 141:243828
GI




I

AB Title compds., e.g., (I), were prepared and tested for use as inhibitors of coagulation factors Xa and VIIa, for treatment of thromboembolic illnesses or tumors. Thus, Fmoc-D-Nva-OH (Nva = norvaline) was reacted with 4-(3-oxo-4-morpholinyl)aniline, the intermediate Fmoc-deprotected, and the product coupled with 4-ethynylaniline to give I. I had IC50 affinities for factor Xa or VIIa receptors, resp., of 2.5 x 10-8 M and 8.8 x 10-8 M (no exptl. details given).

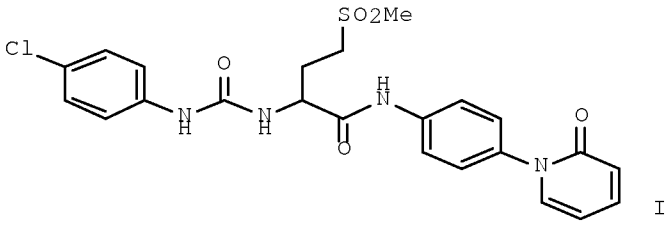
L44 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:605492 HCAPLUS Full-text
DOCUMENT NUMBER: 141:157122
TITLE: Preparation of ureidoazinylalkanamides as inhibitors of blood coagulation Factor VIIa and Xa.
INVENTOR(S): Dorsch, Dieter; Cezanne, Bertram; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes; Van Amsterdam, Christoph
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: Ger. Offen., 25 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10302500 | A1 | 20040729 | DE 2003-10302500 | 20030123 |

| | | | | | |
|---|---|---|---|---|---|
| AU 2004205354 | A1 | 20040805 | AU 2004-205354 | | 20040108 |
| CA 2514100 | A1 | 20040805 | CA 2004-2514100 | | 20040108 |
| WO 2004065369 | A1 | 20040805 | WO 2004-EP61 | | 20040108 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ | | | | | |
| EP 1585730 | A1 | 20051019 | EP 2004-700684 | | 20040108 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| BR 2004006844 | A | 20051213 | BR 2004-6844 | | 20040108 |
| CN 1741996 | A | 20060301 | CN 2004-80002520 | | 20040108 |
| JP 2006516566 | T | 20060706 | JP 2006-500530 | | 20040108 |
| MX 2005PA07715 | A | 20050930 | MX 2005-PA7715 | | 20050720 |
| US 20060074072 | A1 | 20060406 | US 2005-543109 | | 20050722 |
| ZA 2005006730 | A | 20060531 | ZA 2005-6730 | | 20050822 |
| PRIORITY APPLN. INFO.: | | | DE 2003-10302500 | A | 20030123 |
| | | | WO 2004-EP61 | A | 20040108 |

OTHER SOURCE(S): MARPAT 141:157122

GI




I

AB DNHCOXCHR1CONHWYT [D = (substituted) Ph, pyridyl; R1 = (substituted) A; W = [C(R3)2]n; X = NR3, O; Y = alkylene, heterocyclylene, arylene; R2 = H, A, [C(R3)2]nAr, etc.; Ar = (substituted) Ph; R3 = H, A; T = N(R2)2, (substituted) saturated, unsatd., or aromatic carbocyclyl, heterocyclyl; A = (O-, S, or CH:CH-interrupted) (fluorinated) alkyl; n = 0-2], were prepared Thus, 2-amino-4-methylsulfonylbutyric acid in H2O at 80° was treated with 4-chlorophenyl isocyanate followed by stirring for 1 h to give 2-[3-(4-chlorophenyl)ureido]-4-methanesulfonylbutyric acid. This was stirred with 1-(4-aminophenyl)-1H-pyridin-2-one and TBTU in DMF for 24 h to give title compound (I). I bound to Factor Xa receptors with IC50 = 2.8 + 10-8 M.

L44 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2004:450507 HCAPLUS Full-text |
| DOCUMENT NUMBER: | 141:7126 |
| TITLE: | Preparation of heterocyclylamides as inhibitors of Factor VIIA and Xa. |
| INVENTOR(S): | Dorsch, Dieter; Cezanne, Bertram; Mederski, Werner; Tsaklakidis, Christos; Wurziger, Hanns; Gleitz, Johannes; van Amsterdam, Christoph |
| PATENT ASSIGNEE(S): | Merck Patent GmbH, Germany |
| SOURCE: | Ger. Offen., 26 pp.<br>CODEN: GWXXBX |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | German |

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10254336 | A1 | 20040603 | DE 2002-10254336 | 20021121 |
| CA 2506716 | A1 | 20040603 | CA 2003-2506716 | 20031030 |
| WO 2004046138 | A1 | 20040603 | WO 2003-EP12080 | 20031030 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003286145 | A1 | 20040615 | AU 2003-286145 | 20031030 |
| EP 1562939 | A1 | 20050817 | EP 2003-776875 | 20031030 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006512321 | T | 20060413 | JP 2004-552505 | 20031030 |
| US 20060052376 | A1 | 20060309 | US 2005-535246 | 20050518 |

| | | | | |
|---|---|---|---|---|
| PRIORITY APPLN. INFO.: | | | DE 2002-10254336 | A 20021121 |
| | | | WO 2003-EP12080 | W 20031030 |

OTHER SOURCE(S): MARPAT 141:7126
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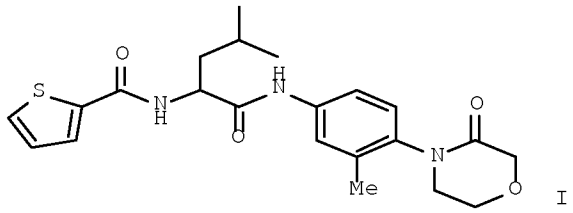


I

AB DXNH[C(R1)2]mCONHWYT [D = (substituted) aryl, heteroaryl; X = CO, C(R3)2; W = [C(R3)2]n; R1 = H, (substituted) A; R3 = H, A; A = (fluoro-substituted) alkyl optionally interrupted by O, S, CH:CH; T = mono- or bicyclic (substituted) (unsatd.) (aromatic) carbocyclyl, heterocyclyl; Y = alkylene, cycloalkylene, (hetero)arylene; m = 1, 2; n = 0-2], were prepared for treatment of thrombosis, arteriosclerosis, inflammation, etc. (no data). Thus, (R)-2-[(5-chlorothiophene-2- carbonyl)amino]-4-methylpentanoic acid (preparation given), 4-(4-amino-2-methylphenyl)morpholin-3-one, and TBTU were stirred 18 h in DMF to give title compound (I).

L44 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:328850 HCAPLUS Full-text
DOCUMENT NUMBER: 140:357340
TITLE: Preparation of N-(5-chloro-2-thienyl)ureas and related compounds as coagulation factor Xa inhibitors for the treatment of thromboembolic illnesses
INVENTOR(S): Dorsch, Dieter; Cezanne, Bertram;

Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10247226 | A1 | 20040422 | DE 2002-10247226 | 20021010 |
| CA 2501706 | A1 | 20040429 | CA 2003-2501706 | 20030918 |
| WO 2004035039 | A1 | 20040429 | WO 2003-EP10400 | 20030918 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003270223 | A1 | 20040504 | AU 2003-270223 | 20030918 |
| EP 1549304 | A1 | 20050706 | EP 2003-750577 | 20030918 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006510604 | T | 20060330 | JP 2004-544033 | 20030918 |
| US 20060135515 | A1 | 20060622 | US 2005-530876 | 20050411 |

PRIORITY APPLN. INFO.: DE 2002-10247226 A 20021010
WO 2003-EP10400 W 20030918

OTHER SOURCE(S): MARPAT 140:357340
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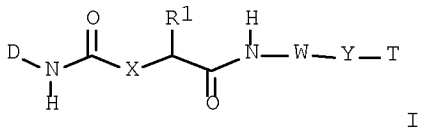


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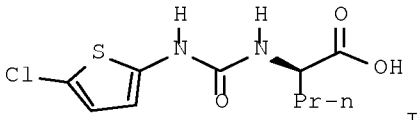


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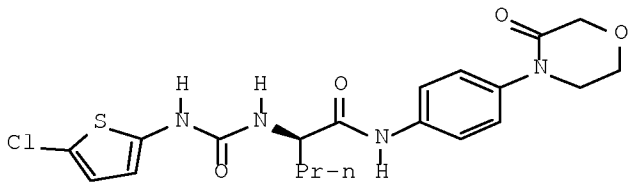


III

AB Title compds. I [D = halo, A, OR2, etc.; X = NR3, O; R1 = H, Ar, cycloalkyl, etc.; R2 = H, A, [C(R3)]n-Ar, etc.; R3 = H, A; W = [C(R3)]n; Y = alkylene, cycloalkylene, Het-diyl (sic), etc.; T = aromatic, heterocyclic; A = OR2, NO2, CN, etc.; n = 0-2] and their pharmaceutically acceptable salts and formulations were prepared For example, coupling of acid II, e.g., prepared from 2-chloro-5-isocyanatothiophene and D-norvaline, and 4-(4-

aminophenyl)morpholin-3-one afforded benzimidazole III. In coagulation factor Xa inhibition assays, 2-examples of compds. I exhibited IC50 values ranging from 6.6-19 x 10-8 M, e.g., the IC50 value of benzimidazole III was 1.9 x 10-7 M. Compds. I are claimed useful for the treatment of thromboembolic illnesses and tumors.

L44 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:177880 HCAPLUS Full-text
DOCUMENT NUMBER: 140:235708
TITLE: Preparation of benzimidazoles as coagulation factor Xa inhibitors for the treatment of thromboembolic illnesses
INVENTOR(S): Dorsch, Dieter; Cezanne, Bertram; Mederski, Werner; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Ger. Offen., 34 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10238002 | A1 | 20040304 | DE 2002-10238002 | 20020820 |
| CA 2496139 | A1 | 20040304 | CA 2003-2496139 | 20030704 |
| WO 2004017963 | A1 | 20040304 | WO 2003-EP7180 | 20030704 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003250890 | A1 | 20040311 | AU 2003-250890 | 20030704 |
| BR 2003013634 | A | 20050621 | BR 2003-13634 | 20030704 |
| EP 1558247 | A1 | 20050803 | EP 2003-792176 | 20030704 |
| EP 1558247 | B1 | 20080220 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1674893 | A | 20050928 | CN 2003-819835 | 20030704 |
| JP 2006500369 | T | 20060105 | JP 2004-529997 | 20030704 |
| AT 386518 | T | 20080315 | AT 2003-792176 | 20030704 |
| US 20050272740 | A1 | 20051208 | US 2005-525001 | 20050217 |
| PRIORITY APPLN. INFO.: | | | DE 2002-10238002 A | 20020820 |
| | | | WO 2003-EP7180 W | 20030704 |

OTHER SOURCE(S): MARPAT 140:235708
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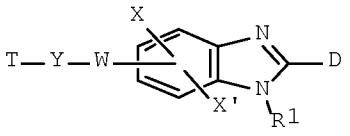

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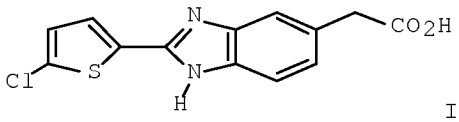

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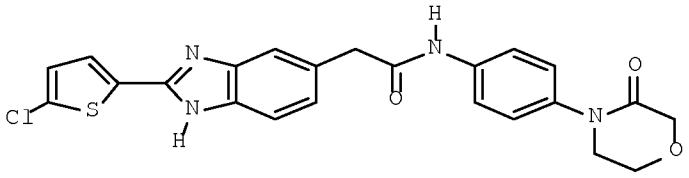

III

AB Title compds. I [D = halo, A, OR2, etc.; X, X' = N, halo, A, etc.; R1 = H, A; R2 = H, A, [C(R1)]n-Ar', etc.; Y = alkylene, cycloalkylene, Het-diyl (sic), etc.; T = aromatic, heterocyclic; W = [C(R2)2]nCONR2[C(R2)2]n, [C(R2)2]nNR2CO[C(R2)2]n, [C(R2)2]nO[C(R2)2]n, etc.; A = (un)substituted alkyl with provisos; Ar' = (un)substituted Ph e.g., halo, A, OR1, etc.; n = 0-2] and their pharmaceutically acceptable salts and formulations were prepared For example, coupling of acid II, e.g., prepared from 2-chlorothiophen-5-aldehyde in 2-steps, and 4-(4-aminophenyl)morpholin-3- one afforded benzimidazole III. In coagulation factor Xa inhibition assays, 3-examples of compds. I exhibited IC50 values ranging from 1.2-2.3 x 10-7 M, e.g., the IC50 value of benzimidazole III was 2.3 x 10-7 M. Compds. I are claimed useful for the treatment of thromboembolic illnesses and tumors.

L44 ANSWER 24 OF 38 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004530089 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15501047
TITLE: Chlorothiophenecarboxamides as P1 surrogates of inhibitors of blood coagulation factor Xa.
AUTHOR: Mederski Werner W K P; Cezanne Bertram; van Amsterdam Christoph; Buhring Karl-Ulrich; Dorsch Dieter; Gleitz Johannes; Marz Joachim; Tsaklakidis Christos
CORPORATE SOURCE: Merck KGaA, Preclinical Pharmaceutical Research, 64271 Darmstadt, Germany.. mederski@merck.de
SOURCE: Bioorganic & medicinal chemistry letters, (2004 Dec 6) Vol. 14, No. 23, pp. 5817-22.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 26 Oct 2004
Last Updated on STN: 23 Mar 2005
Entered Medline: 22 Mar 2005

AB Neutral chlorothiophenecarboxamides bearing an amino acid and a substituted aniline were synthesized and investigated for their factor Xa inhibitory activity in vitro. From selected 2-methylphenyl morpholinones the solution properties were determined. The most soluble and active compounds were then investigated in different animal species to compare the pharmacokinetic parameters. This led to a potent, water soluble and orally bioavailable candidate for further development: EMD 495235.

L44 ANSWER 25 OF 38 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004302259 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15203158
TITLE: Halothiophene benzimidazoles as P1 surrogates of inhibitors of blood coagulation factor Xa.
AUTHOR: Mederski Werner W K R; Dorsch Dieter; Anzali Soheila; Gleitz Johannes; Cezanne Bertram; Tsaklakidis Christos
CORPORATE SOURCE: Merck KGaA, Preclinical Pharmaceutical Research, 64271 Darmstadt, Germany.. mederski@merck.de
SOURCE: Bioorganic & medicinal chemistry letters, (2004 Jul 16) Vol. 14, No. 14, pp. 3763-9.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 24 Jun 2004
Last Updated on STN: 8 Feb 2005
Entered Medline: 7 Feb 2005

AB Neutral weak halothiophene benzimidazole inhibitors of the serine protease factor Xa were identified via screening of a compound library. The X-ray crystal structure of representative 3a bound to human fXa confirmed the S1 binding mode. Starting from 3a a series of halothiophene benzimidazoles was synthesized and investigated for their factor Xa inhibitory activity. This led to potent and selective achiral inhibitors against fXa such as compounds 9k and 9w.

L44 ANSWER 26 OF 38 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:473432 BIOSIS Full-text
DOCUMENT NUMBER: PREV200510263251
TITLE: Novel solubilizing S4-residues for factor XA inhibitors: Synthesis and structure-activity relationships of 1-aryl-2-imino-pyrrrolidine and -piperidine derivatives.
AUTHOR(S): Cezanne, Bertram [Reprint Author]; Dorsch, Dieter; Mederski, Werner W. K. R.; Tsaklakidis, Christos; Gleitz, Johannes; Anzali, Soheila
CORPORATE SOURCE: Merck KGaA, Preclin Res and Dev, D-64271 Darmstadt, Germany
bertram.cezanne@merck.de; dieter.dorsch@merck.de
SOURCE: Abstracts of Papers American Chemical Society, (AUG 22 2004) Vol. 228, No. Part 1, pp. U953.
Meeting Info.: Meeting of the Division of Chemical Toxicology of the American-Chemical-Society held at the 228th National Meeting of the American-Chemical-Society. Philadelphia, PA, USA. August 22 -26, 2004. Amer Chem Soc, Div Chem Toxicol.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

L44 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:658117 HCAPLUS Full-text

TITLE: Novel solubilizing S4-residues for factor Xa inhibitors: Synthesis and structure-activity relationships of 1-aryl-2-imino-pyrrolidine and -piperidine derivatives

AUTHOR(S): Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner W. K. R.; Tsaklakidis, Christos; Gleitz, Johannes; Anzali, Soheila

CORPORATE SOURCE: Preclinical Research & Development, Merck KGaA, Darmstadt, 64271, Germany

SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-253. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Factor Xa is a serine proteinase, which cleaves prothrombin to thrombin, leading to clot formation. It is widely recognized as a very attractive target for the development of new antithrombotic agents. Factor Xa possesses two distinct binding pockets, P1, which has been found to bind hydrophobic chlorophenyl residues well, and P4, which has a more extended shape and binds two-ring S4-residues like biphenyl or heterocyclyl-Ph. In our search for potent and soluble factor Xa inhibitors, we found that compds. with S4-residues bearing a basic cyclic amidine moiety such as 1-aryl-2-imino-pyrrolidine or -piperidine showed both high potency and good aqueous solubility The binding mode of these compds. was studied by X-ray structure anal. of a complex of compound 1 with factor Xa. We will report on the syntheses and biol. properties (in vitro and in vivo) of several factor Xa inhibitors with S4-residues having a cyclic amidine moiety.

L44 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:892749 HCAPLUS Full-text

DOCUMENT NUMBER: 139:381378

TITLE: Preparation of carboxylic acid amides as inhibitors of blood-coagulation factor Xa and VIIa

INVENTOR(S): Dorsch, Dieter; Mederski, Werner; Gleitz, Johannes; Cezanne, Bertram; Tsaklakidis, Christos; Barnes, Christopher

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003093235 | A1 | 20031113 | WO 2003-EP3331 | 20030331 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| DE 10218974 | A1 | 20031127 | DE 2002-10218974 | 20020427 |
| DE 10236868 | A1 | 20040226 | DE 2002-10236868 | 20020812 |
| CA 2483228 | A1 | 20031113 | CA 2003-2483228 | 20030331 |
| AU 2003226755 | A1 | 20031117 | AU 2003-226755 | 20030331 |
| EP 1499591 | A1 | 20050126 | EP 2003-747402 | 20030331 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

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|---|---|---|---|---|
| JP 2005531547 | T | 20051020 | JP 2004-501374 | 20030331 |
| US 20050171154 | A1 | 20050804 | US 2004-512478 | 20041026 |
| US 7183277 | B2 | 20070227 | | |

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|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 2002-10218974 | A | 20020427 |
| | DE 2002-10236868 | A | 20020812 |
| | WO 2003-EP3331 | W | 20030331 |

OTHER SOURCE(S): MARPAT 139:381378

AB Carboxylic acid amides DNHC(O)CHR1C(O)NHWYT [D = (substituted) Ph, pyridyl, thienyl; X = NR3, O; R1 = H, Ar, Het, cycloalkyl, (substituted) A; W = [C(R3)2]n; Y = alkylene, cycloalkylene, Het-diyl, Ar-diyl; T = (bicyclic) (substituted) heterocyclyl; R3 = H, A; A = (branched) (interrupted) (fluorinated) C1-10 alkyl; Ar = (substituted) Ph, naphthyl, biphenyl; Het = (bicyclic) (substituted) heterocyclyl; n = 0-2], were prepared for treating thrombosis and tumors. Thus, (R)-2-[N-(4- chlorophenyl)-carbamoyloxy]-N-[4-(2-iminopiperidin-1-yl)phenyl]-2- phenylacetamide (preparation given) in HCl was lyophilized to give (R)-2-[N-(4-chlorophenyl)-carbamoyloxy]-N-[4-(2-iminopiperidin-1- yl)phenyl]-2-phenylacetamide hydrochloride. The latter showed affinity to the receptor Xa with IC50 = 5.8·10-8 M and to the receptor VIIa with IC50 = 9.9·10-8 M.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

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|---|---|
| ACCESSION NUMBER: | 2003:818282 HCAPLUS Full-text |
| DOCUMENT NUMBER: | 139:323430 |
| TITLE: | Preparation of 2-iminopyrrolidines and related compounds as blood-coagulation factor Xa and VIIa inhibitors for the treatment of tumors and thromboembolic diseases |
| INVENTOR(S): | Cezanne, Bertram; Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Barnes, Christopher; Gleitz, Johannes |
| PATENT ASSIGNEE(S): | Merck Patent G.m.b.H., Germany |
| SOURCE: | PCT Int. Appl., 81 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | German |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003084533 | A1 | 20031016 | WO 2003-EP2349 | 20030307 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| DE 10214832 | A1 | 20031016 | DE 2002-10214832 | 20020404 |
| CA 2481026 | A1 | 20031016 | CA 2003-2481026 | 20030307 |
| AU 2003214102 | A1 | 20031020 | AU 2003-214102 | 20030307 |
| EP 1490056 | A1 | 20041229 | EP 2003-709758 | 20030307 |
| EP 1490056 | B1 | 20060830 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

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|---|---|---|---|---|
| JP 2005528377 | T | 20050922 | JP 2003-581773 | 20030307 |
| AT 337779 | T | 20060915 | AT 2003-709758 | 20030307 |
| ES 2271539 | T3 | 20070416 | ES 2003-709758 | 20030307 |
| US 20050176760 | A1 | 20050811 | US 2004-510046 | 20041001 |

PRIORITY APPLN. INFO.: DE 2002-10214832 A 20020404
WO 2003-EP2349 W 20030307

OTHER SOURCE(S): MARPAT 139:323430

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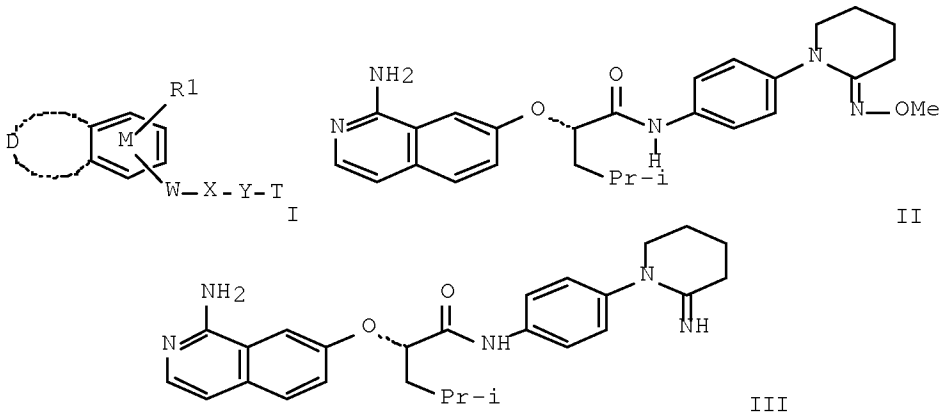


I II III

AB Title compds. I [D = (un)saturated 3-4 membered alkylene (sic) with provisos; M = Ph, aromatic heterocycle containing 1-2 N, O, or S atoms; R1 = H, halo, A, etc.; A = (un)substituted alkyl; W = C(R2)2, [(CR2)2]2, OC(R2)2, etc.; R2 = H, A, [C(R3)2]n-Ar, etc.; R3 = H, A; Ar = (un)substituted aryl, e.g., halo, A, OR3, etc.; X = CONR2, CONR2C(R3)2, C(R3)2NR3, etc.; Y = alkylene, cycloalkylene, Het-diyl (sic), etc.; T = (un)substituted aromatic, heteroarom.; n = 0-2] and their pharmaceutically acceptable salts and formulations were prepared For example, Raney-Ni mediated reduction of hydroxyoxime II, e.g., prepared from 7-isoquinolinol in 4-steps, afforded the diacetate salt of 2-iminopiperidine III. In coagulation factor Xa receptor affinity assays, 5-examples of compds. I exhibited IC50 values ranging from 2.7-0.058 μM, e.g., the IC50 value of 2-iminopiperidine III diacetate was 2.7 μM. Compds. I are claimed useful as antithrombotic and antitumor agents.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:719442 HCAPLUS Full-text
DOCUMENT NUMBER: 139:245786
TITLE: Preparation of semicarbazides as coagulation factor Xa inhibitors for the treatment of thromboembolic diseases

INVENTOR(S): Mederski, Werner; Cezanne, Bertram ; Tsaklakidis, Christos; Dorsch, Dieter; Barnes, Christopher; Gleitz, Johannes

PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003074479 | A1 | 20030912 | WO 2003-EP1177 | 20030206 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2478528 | A1 | 20030912 | CA 2003-2478528 | 20030206 |
| AU 2003206852 | A1 | 20030916 | AU 2003-206852 | 20030206 |
| EP 1480948 | A1 | 20041201 | EP 2003-704559 | 20030206 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003008136 | A | 20050104 | BR 2003-8136 | 20030206 |
| JP 2005519114 | T | 20050630 | JP 2003-572950 | 20030206 |
| CN 1639115 | A | 20050713 | CN 2003-805144 | 20030206 |
| MX 2004PA08479 | A | 20041206 | MX 2004-PA8479 | 20040901 |
| US 20050119316 | A1 | 20050602 | US 2004-506801 | 20040907 |
| ZA 2004007903 | A | 20050704 | ZA 2004-7903 | 20040930 |

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|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 2002-10209211 | A | 20020304 |
| | WO 2003-EP1177 | W | 20030206 |

OTHER SOURCE(S): MARPAT 139:245786

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R = C(=NH)NH2, OH, OCOOA, etc.; R1 = (un)substituted alkyl; R2 = S(O)pA, S(O)pNHA, CF3, etc.; R3 = H, halo; A = H, ; p = 0-2] and their pharmaceutically acceptable salts and formulations were prepared For example, Michael addition of phenylmagnesium bromide to ketone II, e.g., prepared from 3-fluoro-2'-(methylsulfonyl)-[1,1'-biphenyl]-4-amine in 2-steps, followed by hydroxylamine mediated hydrolysis, afforded claimed N-hydroxycarboximidamide III. In coagulation factor Xa affinity receptor (sic) assays, 3-examples of compds. I exhibited IC50 values ranging from 0.028-3.8 μM, e.g., the IC50 value of N-hydroxycarboximidamide III was 3.8 μM. Compds. I are claimed useful as antimigraine, antithrombotic, antiarteriosclerotic, etc. agents.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:376636 HCAPLUS Full-text
DOCUMENT NUMBER: 138:385436
TITLE: Preparation of 4-(1,1-dioxido-2-isothiazolidinyl)benzenamines as inhibitors of blood-coagulation factor Xa for the treatment of thromboembolic diseases
INVENTOR(S): Dorsch, Dieter; Cezanne, Bertram; Tsaklakidis, Christos; Mederski, Werner; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003039543 | A1 | 20030515 | WO 2002-EP11349 | 20021010 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10155075 | A1 | 20030522 | DE 2001-10155075 | 20011109 |
| CA 2465713 | A1 | 20030515 | CA 2002-2465713 | 20021010 |
| AU 2002363366 | A1 | 20030519 | AU 2002-363366 | 20021010 |
| AU 2002363366 | B2 | 20071122 | | |
| EP 1441726 | A1 | 20040804 | EP 2002-802623 | 20021010 |
| EP 1441726 | B1 | 20061220 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002013680 | A | 20041026 | BR 2002-13680 | 20021010 |
| HU 2004001983 | A2 | 20050128 | HU 2004-1983 | 20021010 |
| CN 1582148 | A | 20050216 | CN 2002-821919 | 20021010 |
| JP 2005522412 | T | 20050728 | JP 2003-541834 | 20021010 |
| AT 348611 | T | 20070115 | AT 2002-802623 | 20021010 |
| RU 2301228 | C2 | 20070620 | RU 2004-117594 | 20021010 |
| ES 2277623 | T3 | 20070716 | ES 2002-802623 | 20021010 |
| MX 2004PA04307 | A | 20040811 | MX 2004-PA4307 | 20040506 |
| US 20040254175 | A1 | 20041216 | US 2004-495254 | 20040510 |
| US 7199133 | B2 | 20070403 | | |
| ZA 2004004549 | A | 20050204 | ZA 2004-4549 | 20040608 |
| PRIORITY APPLN. INFO.: | | | DE 2001-10155075 A | 20011109 |
| | | | WO 2002-EP11349 W | 20021010 |

OTHER SOURCE(S): MARPAT 138:385436
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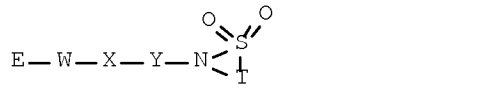

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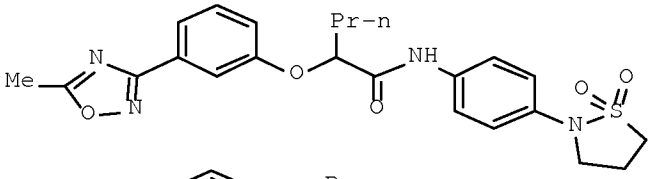

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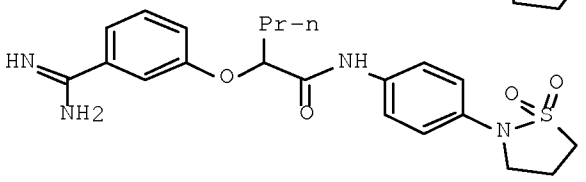

III

AB Title compds. I [E = (un)substituted aryl, heteroaryl; W = C(R2)2, [C(R2)2], OC(R2)2, etc.; R2 = H, A, [C(R3)2]n, etc.; R3 = H, A; X = CONR2, CONR2C(R3)2, C(R3)2NR2, etc.; Y = alkylene, cycloalkylene, Ar-diyl (sic), etc.; Ar = (un)substituted Ph, naphthyl, biphenyl; T = (un)substituted (CH2)p, e.g., N, O, S; n = 0-2; p = 1-6] and their pharmaceutically acceptable salts were prepared For example, Raney-Nickel mediated reduction of oxadiazol II, e.g., prepared from 4-nitroaniline in 4-steps, afforded isothiazolidine III acetate. In blood-coagulation factor Xa inhibition studies, isothiazolidine III acetate exhibited an IC50 value of 3.5 x 10-7 M. Compds. I are claimed useful for the treatment of thromboembolic diseases and tumors.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:133044 HCAPLUS Full-text
DOCUMENT NUMBER: 138:187647
TITLE: Preparation of phenyl derivatives as coagulation factor Xa inhibitors
INVENTOR(S): Dorsch, Dieter; Cezanne, Bertram; Tsaklakidis, Christos; Mederski, Werner; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003013531 | A1 | 20030220 | WO 2002-EP7798 | 20020712 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| DE 10139060 | A1 | 20030220 | DE 2001-10139060 | 20010808 |
| CA 2456717 | A1 | 20030220 | CA 2002-2456717 | 20020712 |
| AU 2002325882 | A1 | 20030224 | AU 2002-325882 | 20020712 |
| AU 2002325882 | B2 | 20070517 | | |
| EP 1414456 | A1 | 20040506 | EP 2002-760242 | 20020712 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002011737 | A | 20040928 | BR 2002-11737 | 20020712 |
| CN 1538845 | A | 20041020 | CN 2002-815482 | 20020712 |
| HU 2004001405 | A2 | 20041228 | HU 2004-1405 | 20020712 |
| JP 2005501075 | T | 20050113 | JP 2003-518540 | 20020712 |
| MX 2004PA01121 | A | 20040520 | MX 2004-PA1121 | 20040204 |
| US 20040235828 | A1 | 20041125 | US 2004-486238 | 20040209 |
| ZA 2004001800 | A | 20050204 | ZA 2004-1800 | 20040304 |

PRIORITY APPLN. INFO.: DE 2001-10139060 A 20010808
WO 2002-EP7798 W 20020712

OTHER SOURCE(S): CASREACT 138:187647; MARPAT 138:187647

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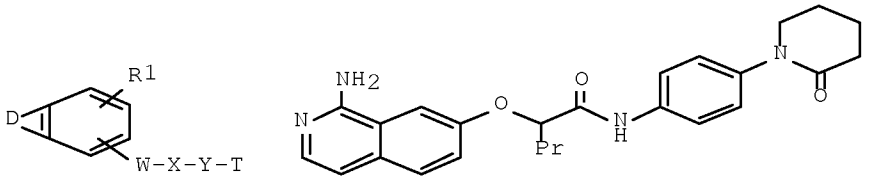



I II

AB Novel Ph compds. I [D = (un)saturated 3 - 4 alkylene chain, containing 1 - 2 N, O and/or S {may be substituted with halogen, A, {C(R3)2}n-Ar, {C(R3)2}n-Het1, {C(R3)2}n-cycloalkyl, OR2, N(R2)2, NO2, CN, CO2R2, CON(R2)2, NR2COA, NR2SO2A, COR2, SO2NR2, S(O)mA}; W = C(R2)2, {C(R2)2}2, OC(R2)2, NR2C(R2)2; X = CONR2, CONR2C(R3)2, C(R3)2NR2, C(R3)2NR2C(R3)2; Y = alkylene, cycloalklylene, Het-diyl, Ar-diyl; T = (un)substituted heterocycle containing 1 - 4 of N, O and/or S; A = (un)branched C1-6-alkyl {may contain O, S, CH:CH or substituted with 1 - 7 F}; R1 = H, halogen, A, OR2, N(R2)2, NO2, CN, CO2R2, CON(R2)2, {C(R3)2}nAr, {C(R3)2}n-Het, {C(R3)2}n-cycloalkyl; R2 = H, A, {C(R3)2}nAr, {C(R3)2}n-Het, {C(R3)2}n-cycloalkyl; R3 = H, A; Ar = (un)substituted Ph, naphthyl, biphenyl {may be substituted with halogen, A, OR3, N(R3)2, NO2, CN, CO2R3, CON(R3)2, NR3COA, NR3CON(R3)2, NR3SO2A, COR3, SO2N(R3)2, SOmA}; Het = (un)saturated or aromatic heterocycle (containing 1 - 4 N, O and/or S and may be substituted with halogen, A, {C(R3)2}n-Het1, {C(R3)2}n-cycloalkyl, OR2, N(R2)2, NO2, CN, CO2R2, CON(R2)2, NR2COA, NR2CON(R2)2, NR2SO2A, COR2, SO2NR2, S(O)mA); Het1 = (un)saturated or aromatic heterocycle {containing 1 - 2 N, O and/or S and may be substituted with halogen, A, OR2, N(R2)2, NO2, CN, CO2R2, CON(R2)2, NR2COA, NR2CON(R2)2, NR2SO2A, COR2, SO2NR2, S(O)mA}; halogen = Cl Br, F, I; n = 0 - 2; m = 0 - 2] are claimed. I and their pharmaceutically acceptable derivs., solvates, stereoisomers and their mixts., are inhibitors of coagulation factor Xa and can be used in the prophylaxis and/or therapy of thromboembolic diseases and in the treatment of tumors. Thus isoquinoline II was prepared from 7-hydroxyisoquinoline via O-alkylation with Me(CH2)2CHBrCO2Et, saponification, amidation with 1-(4-aminophenyl)piperidin-

2-one, isoquinoline N-oxidation, isoquinoline N-oxide amination with pyridine, and reaction with ethanolamine. II was tested for thrombin receptor binding ability [IC50 = 3.5 x 10-7 M vs. FXa; IC50 = 2.2 x 10-7 M vs. TF]. I was used in the preparation of drug formulations (injections, suppositories, solns., solvates, tablets, etc.).

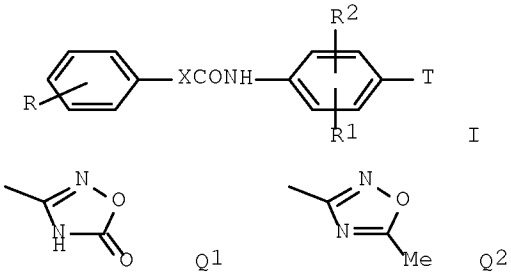
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:891946 HCAPLUS Full-text
DOCUMENT NUMBER: 139:381494
TITLE: Preparation of semicarbazides as inhibitors of blood-coagulation factor Xa and VIIa
INVENTOR(S): Mederski, Werner; Tsaklakidis, Christos; Cezanne, Bertram; Dorsch, Dieter; Barnes, Christopher; Gleitz, Johannes
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10220048 | A1 | 20031113 | DE 2002-10220048 | 20020504 |
| CA 2485065 | A1 | 20031113 | CA 2003-2485065 | 20030407 |
| WO 2003093254 | A1 | 20031113 | WO 2003-EP3581 | 20030407 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003227569 | A1 | 20031117 | AU 2003-227569 | 20030407 |
| EP 1501814 | A1 | 20050202 | EP 2003-724967 | 20030407 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005530754 | T | 20051013 | JP 2004-501393 | 20030407 |
| US 20050171102 | A1 | 20050804 | US 2004-513451 | 20041104 |

PRIORITY APPLN. INFO.: DE 2002-10220048 A 20020504
WO 2003-EP3581 W 20030407

OTHER SOURCE(S): MARPAT 139:381494
GI



I



Q1 Q2

AB Title compds. [I; R = (substituted) C(:NH)NH2, CH2NH2, CONH2, cyano, Q1, Q2; X = N(Ar)NH, NHN(Ar); Ar = (substituted) Ph; R1, R2 = H, A, OH, OA, O(CO)A, halo, CF3, CO2H, CO2A, cyano, CH2NH2, amino, NHA, NA2; A = (branched) (cyclic) C1-10 alkyl; T = (saturated) (substituted) heterocyclyl], were prepd for treating thrombosis and tumors. Thus, a mixture of 1-(3-N-hydroxyamidinophenyl)-4-[3-methyl-4-(2-oxopiperidin-1-yl)phenyl]-1-phenylsemicarbazide (preparation given), Raney-Nickel, HOAc, and H2O in MeOH was stirred over night under H2-atmosphere at room temperature followed by treatment with HCl to give 90% 1-(3-amidinophenyl)-4-[3-methyl-4-(2-oxopiperidin-1-yl)phenyl]-1-phenylsemicarbazide hydrochloride. The latter showed affinity to the receptor Xa with IC50 = 16 E-9 M and to the receptor VIIa with IC50 = 9.8 E-9 M.

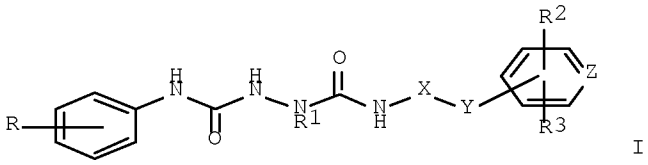
L44 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:736222 HCAPLUS Full-text
DOCUMENT NUMBER: 137:262953
TITLE: Preparation of biurethanes as inhibitors of blood-coagulation factor Xa and VIIa
INVENTOR(S): Mederski, Werner; Cezanne, Bertram; Dorsch, Dieter; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002074735 | A2 | 20020926 | WO 2002-EP2095 | 20020227 |
| WO 2002074735 | A3 | 20031127 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10113402 | A1 | 20020926 | DE 2001-10113402 | 20010320 |

| | | | | |
|---|---|---|---|---|
| CA 2441427 | A1 | 20020926 | CA 2002-2441427 | 20020227 |
| AU 2002253080 | A1 | 20021003 | AU 2002-253080 | 20020227 |
| HU 2003003512 | A2 | 20040128 | HU 2003-3512 | 20020227 |
| EP 1385818 | A2 | 20040204 | EP 2002-722151 | 20020227 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| CN 1498206 | A | 20040519 | CN 2002-806758 | 20020227 |
| JP 2004531494 | T | 20041014 | JP 2002-573744 | 20020227 |
| MX 2003PA08394 | A | 20040129 | MX 2003-PA8394 | 20030917 |
| US 20040097550 | A1 | 20040520 | US 2003-472084 | 20030917 |
| US 6943179 | B2 | 20050913 | | |
| ZA 2003008060 | A | 20040723 | ZA 2003-8060 | 20031016 |
| PRIORITY APPLN. INFO.: | | | DE 2001-10113402 A | 20010320 |
| | | | WO 2002-EP2095 W | 20020227 |

OTHER SOURCE(S): MARPAT 137:262953

GI



I

AB Title compds. [I; R = H, halo, cyano; R1 = H, A, (CH2)nAr; R2 = H, halo; R3 = H, (substituted) Ph, (saturated) aromatic heterocyclyl; X = (CH2)n; Y = absent or piperidin-1,4-diyl; Z = CH, N; A = (branched) (O-, S-, CH:CH-interrupted) (fluorinated) alkyl; Ar = (substituted) Ph; n = 0-2], were prepared Thus, 1-(4-isocyanatophenyl)piperidin-2-one (preparation given) was treated with 78.4 mg N-(4-chlorophenylaminocarbonyl)-N'- phenylhydrazine followed by reflux for 2 h to give 105 mg N-(4-chlorophenylaminocarbonyl)-N'-[4-(2-oxo-1-piperidyl)phenylaminocarbonyl]-N'-phenylhydrazine. The latter showed affinity to the Xa receptor with IC50 = 180 nM/L and to the VIIa receptor with IC50 = 91 nM/L.

L44 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:555466 HCAPLUS Full-text
DOCUMENT NUMBER: 137:125096
TITLE: Preparation of phenyl derivatives containing inhibitors of coagulation factor for prophylaxis and/or therapy of thromboembolic disorders
INVENTOR(S): Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Cezanne, Bertram; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| WO 2002057236 | A1 | 20020725 | WO 2001-EP14296 | 20011205 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10102322 | A1 | 20020725 | DE 2001-10102322 | 20010119 |
| CA 2434937 | A1 | 20020725 | CA 2001-2434937 | 20011205 |
| AU 2002227993 | A1 | 20020730 | AU 2002-227993 | 20011205 |
| AU 2002227993 | B2 | 20070809 | | |
| EP 1351938 | A1 | 20031015 | EP 2001-989580 | 20011205 |
| EP 1351938 | B1 | 20070411 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001016804 | A | 20040217 | BR 2001-16804 | 20011205 |
| CN 1518541 | A | 20040804 | CN 2001-823061 | 20011205 |
| JP 2004535362 | T | 20041125 | JP 2002-557917 | 20011205 |
| HU 2005000110 | A2 | 20050628 | HU 2005-110 | 20011205 |
| AT 359271 | T | 20070515 | AT 2001-989580 | 20011205 |
| ES 2284718 | T3 | 20071116 | ES 2001-989580 | 20011205 |
| MX 2003PA06483 | A | 20030922 | MX 2003-PA6483 | 20030718 |
| IN 2003KN01033 | A | 20060602 | IN 2003-KN1033 | 20030813 |
| ZA 2003006419 | A | 20041118 | ZA 2003-6419 | 20030818 |
| US 20040087582 | A1 | 20040506 | US 2003-466680 | 20031218 |
| US 7273867 | B2 | 20070925 | | |
| PRIORITY APPLN. INFO.: | | | DE 2001-10102322 A | 20010119 |
| | | | WO 2001-EP14296 W | 20011205 |

OTHER SOURCE(S): MARPAT 137:125096

AB Novel compds. of the formula R1R2C6H3-W-X-Y-T in which W, X, Y, T, R1 and R2 are as defined in Patent Claim 1, are inhibitors of coagulation factor Xa and can be employed for the prophylaxis and/or therapy of thromboembolic disorders. Thus, 3-(5-methyl-1,2,4-oxadiazol-3-yl)phenol wa reacted with Et 2-bromovalerate, sodium hydroxide, thionyl chloride, 4-morpholin-4-ylaniline, followed a hydrogenation in acetic acid to give 2-(3-amidinophenoxy)-N-(4-morpholin-4-ylphenyl)valeramide acetate, showing IC50=3x10-7 M and IC50=4.9x10-7 M.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:465965 HCAPLUS Full-text

DOCUMENT NUMBER: 137:47128

TITLE: Preparation of of ureido- and carbamoyloxy-substituted amides as inhibitors of factor Xa for the treatment of clotting disorders and tumors.

INVENTOR(S): Dorsch, Dieter; Mederski, Werner; Tsaklakidis, Christos; Cazanne, Bertram; Gleitz, Johannes; Barnes, Christopher

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002048099 | A1 | 20020620 | WO 2001-EP13545 | 20011121 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10063008 | A1 | 20020620 | DE 2000-10063008 | 20001216 |
| CA 2431766 | A1 | 20020620 | CA 2001-2431766 | 20011121 |
| AU 2002021881 | A | 20020624 | AU 2002-21881 | 20011121 |
| EP 1341755 | A1 | 20030910 | EP 2001-270524 | 20011121 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001016115 | A | 20031223 | BR 2001-16115 | 20011121 |
| HU 2003003296 | A2 | 20040128 | HU 2003-3296 | 20011121 |
| HU 2003003296 | A3 | 20060428 | | |
| JP 2004515538 | T | 20040527 | JP 2002-549632 | 20011121 |
| NO 2003002695 | A | 20030613 | NO 2003-2695 | 20030613 |
| MX 2003PA05342 | A | 20031006 | MX 2003-PA5342 | 20030613 |
| US 20040038858 | A1 | 20040226 | US 2003-450651 | 20030616 |
| IN 2003KN00896 | A | 20050311 | IN 2003-KN896 | 20030714 |
| ZA 2003005455 | A | 20040826 | ZA 2003-5455 | 20030715 |
| US 20050137230 | A1 | 20050623 | US 2005-59655 | 20050217 |

| | | | | |
|---|---|---|---|---|
| PRIORITY APPLN. INFO.: | | DE 2000-10063008 | A | 20001216 |
| | | WO 2001-EP13545 | W | 20011121 |
| | | US 2003-450651 | A3 | 20030616 |

OTHER SOURCE(S): MARPAT 137:47128

AB DNHCOXCHR1CONH(CH2)nEW [D = (substituted) Ph, pyridyl; R1 = H, Ar, Het, cycloalkyl, (substituted) A; R2 = H, A; E = (substituted) phenylene, piperidin-1,4-diyl; W = Ar, Het, N(R2)2, R2, cycloalkyl; X = NH, O; A = (fluoro-substituted) (O-, S-, or CH:CH-interrupted) alkyl; Ar = (substituted) Ph; Het = (aromatic) (substituted) heterocyclyl; n = 0, 1], were prepared Thus, Z-D-Phe-OH, 2'-methylsulfonylbiphenyl-4-ylamine, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, 1-hydroxybenzotriazole, and 4-methylmorpholine were stirred 40 h in DMF to give benzyl [(R)-1-(2'-methylsulfonylbiphenyl-4-ylcarbamoyl)-2-phenylethyl]carbamate. This was hydrogenolyzed in MeOH over Pd/C and the product was stirred with 4-chlorophenyl isocyanate in CH2Cl2 to give (R)-2-[3-(4-chlorophenyl)ureido]-N-(2'-methylsulfonylbiphen-4-yl)-3-phenylpropionamide. The latter inhibited factor Xa with IC50 = 8.6 + 10-8 M.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:791975 HCAPLUS Full-text

DOCUMENT NUMBER: 137:310701

TITLE: Preparation of ethanediamides as inhibitors of blood coagulation factor Xa for the treatment of thromboembolic illnesses

INVENTOR(S): Mederski, Werner; Cezanne, Bertram; Dorsch, Dieter; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: Ger. Offen., 34 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10117823 | A1 | 20021017 | DE 2001-10117823 | 20010410 |
| CA 2445538 | A1 | 20021024 | CA 2002-2445538 | 20020318 |
| WO 2002083630 | A1 | 20021024 | WO 2002-EP2963 | 20020318 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002308166 | A1 | 20021028 | AU 2002-308166 | 20020318 |
| EP 1377543 | A1 | 20040107 | EP 2002-761892 | 20020318 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| HU 2003003733 | A2 | 20040301 | HU 2003-3733 | 20020318 |
| CN 1514823 | A | 20040721 | CN 2002-811605 | 20020318 |
| US 20040220411 | A1 | 20041104 | US 2003-474969 | 20031016 |
| BR 2003004917 | A | 20050614 | BR 2003-4917 | 20031016 |
| ZA 2003008669 | A | 20050207 | ZA 2003-8669 | 20031106 |
| MX 2003PA10205 | A | 20040310 | MX 2003-PA10205 | 20031107 |

PRIORITY APPLN. INFO.: DE 2001-10117823 A 20010410
WO 2002-EP2963 W 20020318

OTHER SOURCE(S): MARPAT 137:310701
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1, R3 = H, aryl, aryl-alkyl, etc.; R2 = aryl, Het; R4 = H, OH, O-aryl, etc.; X = aryl, aryl-alkyl, etc.; aryl = (un)substituted Ph, naphthyl, biphenyl; Het = (un)substituted aromatic heterocyclic with 1-4 N, O and/or S atoms; with provisos], their pharmaceutically acceptable salts and formulations were prepared For example, Ra-Ni/H2 reduction of oxadiazole II, prepared from 3-[3-(bromomethyl)phenyl]-5-methyl-1,2,4- oxadiazole in 6-steps, followed by amine deprotection afforded carboximidamide III.TFA. In inhibition studies of blood coagulation factor Xa, 7-specific examples of I exhibited IC50 values ranging from 6.0 μM - 9.6 nM, e.g., IC50 of carboximidamide III.TFA = 10 nM. Approx. 71-specific examples of compds. I and 52-intermediates were prepared

L44 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:714060 HCAPLUS Full-text
DOCUMENT NUMBER: 137:232677
TITLE: Preparation of heterocyclylphenyls for treatment of thromboembolic diseases and tumors

INVENTOR(S): Mederski, Werner; Cezanne, Bertram ; Dorsch, Dieter; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10112768 | A1 | 20020919 | DE 2001-10112768 | 20010316 |
| CA 2440954 | A1 | 20020926 | CA 2002-2440954 | 20020227 |
| WO 2002074765 | A1 | 20020926 | WO 2002-EP2092 | 20020227 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
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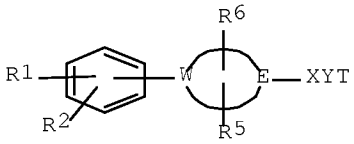
| AU 2002249246 | A1 | 20021003 | AU 2002-249246 | 20020227 |
| EP 1368341 | A1 | 20031210 | EP 2002-718165 | 20020227 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| HU 2003003539 | A2 | 20040128 | HU 2003-3539 | 20020227 |
| CN 1496361 | A | 20040512 | CN 2002-806536 | 20020227 |
| JP 2004527514 | T | 20040909 | JP 2002-573774 | 20020227 |
| MX 2003PA08216 | A | 20040129 | MX 2003-PA8216 | 20030911 |
| US 20040082563 | A1 | 20040429 | US 2003-471768 | 20030916 |
| ZA 2003008028 | A | 20050117 | ZA 2003-8028 | 20031015 |
| PRIORITY APPLN. INFO.: | | | DE 2001-10112768 A | 20010316 |
| | | | WO 2002-EP2092 W | 20020227 |

OTHER SOURCE(S): MARPAT 137:232677
GI




I

AB Title compds. [I; R1 = H, cyano, (substituted) C(:NH)NH2, CON(R3)2, [C(R4)2]nN(R3)2, etc.; R2, R5, R6 = H, halo, A, OR3, N(R3)2, NO2, cyano, [C(R4)2]nAr, [C(R4)2]nHet, [C(R4)2]ncycloalkyl, etc; R3 = H, A, [C(R4)2]nAr, [C(R4)2]nHet, [C(R4)2]ncycloalkyl; R4 = H, A; W = N, CR3; EW = 3-7 membered (substituted) (saturated) (benzo-, heterocyclyl-condensed) (hetero)cyclyl; X = [C(R4)2]nCONR3[C(R4)2]n, [C(R4)2]nNR3CO[C(R4)2]n, etc; Y = alkylene, cycloalkylene, heterocyclyldiyl, aryldiyl; T = (substituted) (bi)heterocyclyl; A = (branched) (O-, S-, CH:CH-interrupted) (fluorinated) C1-6 alkyl; Ar = (substituted) Ph, naphthyl, biphenyl; Het = (substituted) (aromatic)

(bi)heterocyclyl; n = 0-2], were prepd as inhibitors of factor Xa and VIIa (no data). Thus, a mixture of 4-(tert-butoxycarbonyl)-1-(3-cyanophenyl)piperazine-2-carboxylic acid, 1-(4-aminophenyl)piperidin-2- one, N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride, and hydroxybenzotriazole hydrate in DMF was stirred with 4-methylmorpholine for 18 h at room temperature to give 4-(3-cyanophenyl)-3-[4-(2-oxopiperidin-1-yl)phenylcarbamoyl]piperazine-1-carboxylic acid tert-Bu ester which was stirred with DMSO, K2CO3, and H2O2 in MeOH for 2 h at room temperature to give (3-carbamoylphenyl)-3-[4-(2-oxopiperidin-yl)phenylcarbamoyl]piperazine-1-carboxylic acid tert-Bu ester. The latter was treated with HCl in dioxane for 1 h to give 1-[(3-carbamoylphenyl)-piperazin-2-yl]-N-[4-(2- oxopiperidin-1-yl)phenyl]amide.

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=> dis his nofile

     (FILE 'HOME' ENTERED AT 15:33:08 ON 18 JUN 2008)

     FILE 'REGISTRY' ENTERED AT 15:33:26 ON 18 JUN 2008
L1             STR
L2           50 SEA SSS SAM L1
L3             STR L1
L4           47 SEA SSS SAM L3
L5          746 SEA SSS FUL L3
               D L5 QUE STAT

     FILE 'HCAPLUS' ENTERED AT 15:37:04 ON 18 JUN 2008
L6           16 SEA ABB=ON  PLU=ON  L5/P
               D 1-16 IBIB ABS HITSTR

     FILE 'REGISTRY' ENTERED AT 15:39:04 ON 18 JUN 2008
               D L5 QUE STAT

     FILE 'HCAPLUS' ENTERED AT 15:39:04 ON 18 JUN 2008
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     FILE 'REGISTRY' ENTERED AT 15:40:22 ON 18 JUN 2008
L7             STR
L8             STR
L9           42 SEA SSS SAM L7
L10          50 SEA SSS SAM L8

     FILE 'CASREACT' ENTERED AT 15:41:29 ON 18 JUN 2008
L11            STR L7
L12           0 SEA SSS SAM L11 (     0 REACTIONS)
L13           5 SEA SSS FUL L11 (    10 REACTIONS)
               D L13 QUE STAT
               D 1-5 IBIB ABS FHIT

     FILE 'MEDLINE, BIOSIS, EMBASE, HCAPLUS' ENTERED AT 15:45:51 ON 18 JUN 2008
L14           9 SEA ABB=ON  PLU=ON  MEDERSKI W?/AU
L15          43 SEA ABB=ON  PLU=ON  MEDERSKI W?/AU
L16          21 SEA ABB=ON  PLU=ON  MEDERSKI W?/AU
L17         144 SEA ABB=ON  PLU=ON  MEDERSKI W?/AU
     TOTAL FOR ALL FILES
L18         217 SEA ABB=ON  PLU=ON  MEDERSKI W?/AU
L19           2 SEA ABB=ON  PLU=ON  TSAKLAKIDIS C?/AU
L20          17 SEA ABB=ON  PLU=ON  TSAKLAKIDIS C?/AU
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L21             2 SEA ABB=ON  PLU=ON  TSAKLAKIDIS C?/AU
L22            78 SEA ABB=ON  PLU=ON  TSAKLAKIDIS C?/AU
     TOTAL FOR ALL FILES
L23            99 SEA ABB=ON  PLU=ON  TSAKLAKIDIS C?/AU
L24            11 SEA ABB=ON  PLU=ON  DORSCH D?/AU
L25            47 SEA ABB=ON  PLU=ON  DORSCH D?/AU
L26            16 SEA ABB=ON  PLU=ON  DORSCH D?/AU
L27           185 SEA ABB=ON  PLU=ON  DORSCH D?/AU
     TOTAL FOR ALL FILES
L28           259 SEA ABB=ON  PLU=ON  DORSCH D?/AU
L29             4 SEA ABB=ON  PLU=ON  CEZANNE B?/AU
L30            10 SEA ABB=ON  PLU=ON  CEZANNE B?/AU
L31             4 SEA ABB=ON  PLU=ON  CEZANNE B?/AU
L32            48 SEA ABB=ON  PLU=ON  CEZANNE B?/AU
     TOTAL FOR ALL FILES
L33            66 SEA ABB=ON  PLU=ON  CEZANNE B?/AU
L34            26 SEA ABB=ON  PLU=ON  GLEITZ J?/AU
L35            39 SEA ABB=ON  PLU=ON  GLEITZ J?/AU
L36            31 SEA ABB=ON  PLU=ON  GLEITZ J?/AU
L37            83 SEA ABB=ON  PLU=ON  GLEITZ J?/AU
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L38           179 SEA ABB=ON  PLU=ON  GLEITZ J?/AU
L39             2 SEA ABB=ON  PLU=ON  L14 AND L19 AND L24 AND L29 AND L34
L40             6 SEA ABB=ON  PLU=ON  L15 AND L20 AND L25 AND L30 AND L35
L41             2 SEA ABB=ON  PLU=ON  L16 AND L21 AND L26 AND L31 AND L36
L42            34 SEA ABB=ON  PLU=ON  L17 AND L22 AND L27 AND L32 AND L37
     TOTAL FOR ALL FILES
L43            44 SEA ABB=ON  PLU=ON  L18 AND L23 AND L28 AND L33 AND L38
L44            38 DUP REM L43 (6 DUPLICATES REMOVED)
                  D 1-38 IBIB ABS

=> d l5 que stat;d l13 que stat
L3                STR
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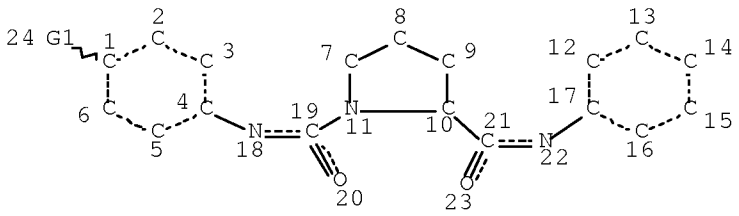


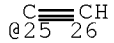


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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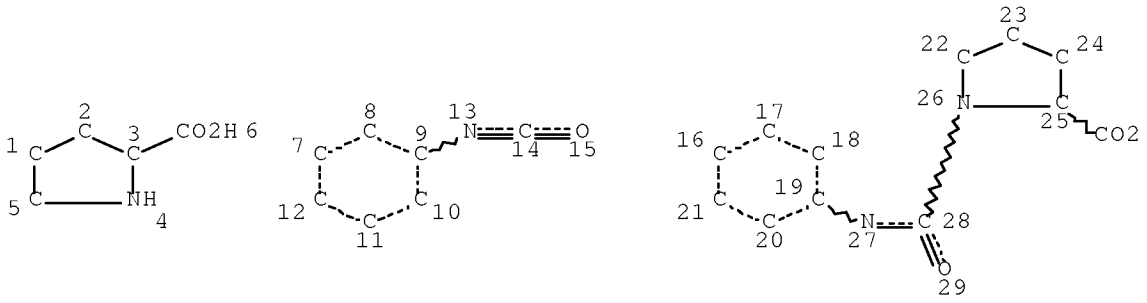
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  26

STEREO ATTRIBUTES: NONE
L5          746 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED    1364 ITERATIONS                          746 ANSWERS
SEARCH TIME: 00.00.01

L11             STR



Page 1-A

H 30

Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  30

STEREO ATTRIBUTES: NONE
L13           5 SEA FILE=CASREACT SSS FUL L11 (    10 REACTIONS)

100.0% DONE     117 VERIFIED      10 HIT RXNS                     5 DOCS
SEARCH TIME: 00.00.01

=> log y

STN INTERNATIONAL LOGOFF AT 15:47:08 ON 18 JUN 2008